**UNITED STATES ENVIRONMENTAL PROTECTION AGENCY**
**WASHINGTON, D.C. 20460**

**OFFICE OF CHEMICAL SAFETY AND POLLUTION PREVENTION**

**MEMORANDUM**

**Date:** September 23, 2011

**SUBJECT:** Fluopyram. Application for Section 3 Registration for Use on Apple, Banana (Import only), Dried Beans, Cherry, Grape (Wine Production only), Peanut, Pistachio, Potato, Sugar Beet, Strawberry, Tree Nuts Crop Group 14, Watermelon, and Rotational Crops Alfalfa, Canola, Cotton, Cereal Grains Crop (Except Rice) Group 15, and Forage, Fodder, and Straw of Cereal Grains Crop (Except Rice) Group 16. Summary of Analytical Chemistry and Residue Data.

**PC Code:** 080302
**Decision No.:** 402628
**Petition No.:** 8F7463
**Risk Assessment Type:** NA
**TXR No.:** NA
**MRID No.:** See MRID Summary Table

**DP Barcodes:** D387587, 389081
**Registration No.:** 264-RNTI
**Regulatory Action:** Section 3 Registration
**Case No.:** NA
**CAS No.:** 658066-35-4
**40 CFR:** To be determined

Ver.Apr.08

**FROM:** Leung Cheng, Chemist
Risk Assessment Branch III
Health Effects Division (7509P)

**THROUGH:** Paula Deschamp, Chief
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**TO:** Cynthia Giles-Parker, Chief
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Registration Division (7505P)

| **MRID Summary Table** | | | |
|---|---|---|---|
| **MRID No.** | **Study Type** | **Monograph Section; Comments** | |
| | | **1st Entry Monograph** | **2nd Entry Monograph** |
| 47372524 | 860.1300 Grape | B.7.1.1 | |
| 47372525 | 860.1300 Grape | B.7.1.1 | |
| 47372526 | 860.1300 Bean | B.7.1.3 | |
| 47372527 | 860.1300 Bean | B.7.1.3 | |
| 47372528 | 860.1300 Potato | B.7.1.2 | |
| 47372529 | 860.1300 Potato | B.7.1.2 | |
| 47372530 | 860.1300 Red pepper | B.7.1.4 | |

| MRID Summary Table | | | |
|---|---|---|---|
| MRID No. | Study Type | Monograph Section; Comments | |
| | | 1st Entry Monograph | 2nd Entry Monograph |
| 47372531 | 860.1300 Red pepper | B.7.1.4 | |
| 47372532 | 860.1300 Laying hen | B.7.2.1 | |
| 47372533 | 860.1300 Laying hen | B.7.2.1 | |
| 47372534 | 860.1300 Lactating goat | B.7.2.2 | |
| 47372535 | 860.1300 Lactating goat | B.7.2.2 | |
| 47372536 | 860.1300 Cell cultures | B.7.1.5 | |
| 47372537 | 860.1340 Crop commodities | B.5.2.1 | |
| 47372538 | 860.1340 Crop commodities | B.5.2.1 | |
| 47372539 | 860.1340 Extraction efficiency | B.5.2.1 | |
| 47372540 | 860.1340 Livestock commodities | B.5.2.2 | |
| 47372541 | 860.1340 Livestock commodities | B.5.2.2 | |
| 47372542 | 860.1340 Livestock commodities | B.5.2.2 | |
| 47372543 | 860.1340 Crop commodities | B.5.2.1; reviewed by Germany | |
| 47372544 | 860.1340 Crop commodities | B.5.2.1; reviewed by Germany | |
| 47372545 | 860.1340 Crop commodities | B.5.2.1; reviewed by Germany | |
| 47372546 | 860.1340 Crop commodities | B.5.2.1 | |
| 47372547 | 860.1340 Waiver request (radiovalidation) | B.5.2.1 | |
| 47372548 | 860.1360 Multiresidue Methods | B.5.2 | |
| 47372549 | 860.1380 Crop commodities | B.7.6.2 | |
| 47372550 | 860.1380 Orange | B.7.6.2 | |
| 47372601 | 860.1480 Cattle | B.7.8.1 | |
| 47372602 | 860.1480 Hen | B.7.8.2 | |
| 47372603 | 860.1500 Fruiting vegetable | B.5.2.1, B.7.6.1 | B.7.6.1 |
| 47372604 | 860.1500 Grape | B.7.6.1 | |
| 47372605 | 860.1500 Strawberry | B.7.6.1, B.7.7.2 | |
| 47372606 | 860.1500 Grasses | | B.7.6.1 |
| 47372608 | 860.1500 Tomato (Europe) | B.7.6.1 | |
| 47372610 | 860.1500 Tomato (Europe) | | |
| 47372615 | 860.1500 Strawberry (Europe) | B.7.6.1 | |
| 47372622 | 860.1520 Grape | B.7.7.2 | |
| 47372623 | 860.1520 Tomato | B.7.7.2 | |
| 47372624 | 860.1520 Strawberry (Europe) | B.7.7.2 | |
| 47372625 | 860.1520 Strawberry (Europe) | | |
| 47372626 | 860.1520 Raisin (Europe) | B.7.7.2 | |
| 47372627 | 860.1520 Wine (Europe) | B.7.7.2 | |
| 47372628 | 860.1520 Wine (Europe) | | |
| 47372629 | 860.1520 Tomato (Europe) | B.7.7.2 | |
| 47372630 | 860.1520 Tomato (Europe) | | |
| 47372631 | 860.1850 Confined rotational crops | B.7.9.1 | |
| 47372632 | 860.1850 Confined rotational crops | B.7.9.1 | |
| 47372633 | 860.1900 Field rotational crops (Europe) | B.7.9.2 | |

| **MRID Summary Table** | | | |
|---|---|---|---|
| **MRID No.** | **Study Type** | **Monograph Section; Comments** | |
| | | **1st Entry Monograph** | **2nd Entry Monograph** |
| None assigned; Document No. M-296625-01 | 860.1900 Field rotational crops (Europe) | | |
| None assigned; Document No. M-296652-01 | 860.1900 Field rotational crops (Europe) | | |
| None assigned; Document No. M-296671-01 | 860.1900 Field rotational crops (Europe) | | |
| 47567010 | 860.1500 Sugar beet and turnip | | B.7.6.1 |
| 47567011 | 860.1500 Root vegetables except sugar beet | | B.7.6.1 |
| 47567012 | 860.1500 Potato | | B.7.6.1 |
| 47567013 | 860.1500 Canola | | B.7.6.1 |
| 47567014 | 860.1500 Field and sweet corn | | B.7.6.1 |
| 47567015 | 860.1500 Wheat and sorghum | | B.7.6.1 |
| 47567016 | 860.1500 Soybean | | B.7.6.1 |
| 47567017 | 860.1500 Hops | | B.7.6.1 |
| 47567018 | 860.1500 Sunflower | | B.7.6.1 |
| 47567019 | 860.1500 Peanut | | B.7.6.1 |
| 47567020 | 860.1500 Tree nuts | | B.7.6.1 |
| 47567021 | 860.1500 Dry bulb onions | | B.7.6.1 |
| 47567022 | 860.1500 Green onions | | B.7.6.1 |
| 47567023 | 860.1500 Leafy vegetables | | B.7.6.1, B.7.7.2 |
| 47567024 | 860.1500 Artichoke (globe) | | B.7.6.1 |
| 47567025 | 860.1500 Head and stem Brassica | | B.7.6.1, B.7.7.2 |
| 47567026 | 860.1500 Leafy Brassica greens | | B.7.6.1, B.7.7.2 |
| 47567027 | 860.1500 Edible-podded legume vegetables | | B.7.6.1 |
| 47567028 | 860.1500 Succulent shelled pea and bean | | B.7.6.1 |
| 47567029 | 860.1500 Dried shelled pea and bean | | B.7.6.1 |
| 47567030 | 860.1500 Cucurbit vegetables | | B.7.6.1 |
| 47567031 | 860.1500 Citrus fruit | | B.7.6.1 |
| 47567032 | 860.1500 Pome fruit | | B.7.6.1 |
| 47567033 | 860.1500 Stone fruit | | B.7.6.1 |
| 47567034 | 860.1500 Caneberry | | B.7.6.1 |
| 47567035 | 860.1500 Bushberry | | B.7.6.1 |
| 47567036 | 860.1500 Banana | | B.7.6.1 |
| 47567037 | 860.1500 Herbs | | B.7.6.1 |
| 47567101 | 860.1500 Dill seed | | B.7.6.1 |
| 47567111 | 860.1520 Apple | | B.7.7.2 |
| 47567112 | 860.1520 Orange | | B.7.7.2 |
| 47567113 | 860.1520 Plum | | B.7.7.2 |
| 47567114 | 860.1520 Peanut | | B.7.7.2 |
| 47567115 | 860.1500/1520 Wheat | | B.7.7.2 |
| 47567116 | 860.1520 Canola | | B.7.7.2 |
| 47567117 | 860.1500/1520 Field corn | | B.7.7.2 |
| 47567118 | 860.1520 Potato | | B.7.7.2 |

| MRID Summary Table | | | |
|---|---|---|---|
| **MRID No.** | **Study Type** | **Monograph Section; Comments** | |
| | | **1st Entry Monograph** | **2nd Entry Monograph** |
| 47567119 | 860.1500/1520 Soybean | | B.7.7.2 |
| 47567120 | 860.1520 Sugar beet | | B.7.7.2 |
| 47567121 | 860.1520 Sunflower | | B.7.7.2 |
| 47567122 | 860.1520 Cotton | | B.7.7.2 |
| 47567123 | 860.1900 Limited field rotational crop study | | B.7.9.2 |
| 47567124 | 860.1900 Rotated alfalfa | | B.7.9.2 |
| 47567125 | 860.1900 Rotated cotton | | B.7.9.2 |

This document was originally prepared under contract by Dynamac Corporation (1901 Research Boulevard, Suite 220; Rockville, MD 20850).

The document has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

## Executive Summary

Fluopyram (AE C656948) is a new fungicide with a broad spectrum of activity against numerous fungal diseases, including Ascomycetes, leaf spots, molds, scab, Alternaria, Septoria, Monlinia, Botrytis, Sclerotinia, and powdery mildews, in a wide range of crops and plants. Fluopyram represents a new class of chemistry (pyridylethylamide), and its biochemical mode of action has been shown to rely on the inhibition of the enzyme succinate dehydrogenase (complex II) within the fungal mitochondrial respiratory chain, thus blocking electron transport. Fluopyram is a Group 7 fungicide.

In 2008, Bayer CropScience submitted a petition proposing the establishment of tolerances for residues of fluopyram (N-[2-[3-chloro-5-(trifluoromethyl)-2-pyridinyl]ethyl]-2-(trifluoromethyl)benzamide) in/on the following crop commodities:

Alfalfa, forage ........ 0.25 ppm
Alfalfa, hay ........ 0.80 ppm
Almond, hulls ........ 8.0 ppm
Apple, wet pomace ........ 2.5 ppm
Artichoke ........ 2.0 ppm
Banana ........ 1.0 ppm
Beet, sugar, roots ........ 0.10 ppm
Berry, lowgrowing, subgroup 13-07G ........ 2.0 ppm
Brassica, head and stem, subgroup 5A ........ 3.0 ppm
Brassica, leafy greens, subgroup 5B ........ 35 ppm
Bushberries, subgroup 13-07B ........ 10 ppm
Caneberries, subgroup 13-07A ........ 5.0 ppm
Citrus, oil ........ 10 ppm
Corn, sweet, kernel plus cob with husk removed ........ 0.10 ppm
Cotton, gin byproducts ........ 0.05 ppm
Cotton, undelinted seed ........ 0.10 ppm
Fruit, citrus, group 10 ........ 1.0 ppm
Fruit, pome, group 11 ........ 1.0 ppm
Fruit, small, vine, climbing, except fuzzy kiwifruit, subgroup 13-07F ...... 2.0 ppm
Fruit, stone, group 12 ........ 2.0 ppm
Grain, cereal, forage, fodder and straw, group 16, except rice; forage ....... 8.0 ppm
Grain, cereal, forage, fodder and straw, group 16, except rice; hay, straw and stover ........ 14 ppm
Grain, cereal, forage, fodder and straw, group 16, except rice; aspirated fractions ........ 50 ppm
Grain, cereal, group 15, except rice and sweet corn ........ 3.0 ppm
Grape, raisin ........ 3.5 ppm
Grass, forage, fodder and hay, group 17; forage ........ 80 ppm
Grass, forage, fodder and hay, group 17; hay ........ 30 ppm
Herbs, subgroup 19A, fresh ........ 50 ppm
Herbs, subgroup 19A, dried ........ 260 ppm
Hop, dried cones ........ 100 ppm
Nut, tree, group 14 (including pistachio) ........ 0.05 ppm
Okra ........ 8.0 ppm
Oilseed, group 20, except cotton ........ 5.0 ppm
Onion, bulb, subgroup 3-07A ........ 0.30 ppm

Onion, green, subgroup 3-07B ........................................................... 20 ppm
Peanut ........................................................................................... 0.05 ppm
Peanut, hay ..................................................................................... 50 ppm
Pepper, non-bell ............................................................................. 8.0 ppm
Potato, processed potato waste ................................................... 0.15 ppm
Soybean, aspirated fractions ......................................................... 70 ppm
Soybean, forage ............................................................................. 8.0 ppm
Soybean, hay .................................................................................. 30 ppm
Soybean, hulls ................................................................................ 0.40 ppm
Soybean, seed ................................................................................ 0.30 ppm
Spices, except black pepper, subgroup 19B ................................ 100 ppm
Vegetable, cucurbit, group 9 ......................................................... 1.0 ppm
Vegetable, foliage of legume, except soybean, subgroup 7A; forage ......... 30 ppm
Vegetable, foliage of legume, except soybean, subgroup 7A; hay ............. 75 ppm
Vegetable, foliage of legume, except soybean, subgroup 7A; vines ........... 16 ppm
Vegetable, fruiting, except non-bell pepper, group 8 ................................ 1.0 ppm
Vegetable, leafy, except Brassica, group 4 ................................................ 35 ppm
Vegetable, leaves of root and tuber, group 2 .............................................. 30 ppm
Vegetable, legume, edible podded, subgroup 6A ...................................... 2.0 ppm
Vegetable, legume, succulent shelled, subgroup 6B ................................ 0.20 ppm
Vegetable, pea and bean, dried shelled (except soybean), subgroup 6C .. 0.50 ppm
Vegetable, root and tuber, except sugarbeet, subgroup 1B ....................... 0.50 ppm
Vegetable, tuberous and corm, subgroup 1C ........................................... 0.05 ppm

In addition, Bayer has proposed tolerances for residues of fluopyram and its metabolite 2-(trifluoromethyl)benzamide, expressed in parent equivalents, in the following livestock commodities:

Cattle, fat ........................................................................................ 0.10 ppm
Cattle, meat ..................................................................................... 0.10 ppm
Cattle, meat byproducts, except liver ........................................... 0.10 ppm
Cattle, liver ...................................................................................... 1.2 ppm
Eggs ................................................................................................ 0.10 ppm
Goat, fat .......................................................................................... 0.10 ppm
Goat, meat ...................................................................................... 0.10 ppm
Goat, meat byproducts, except liver ............................................ 0.10 ppm
Goat, liver ....................................................................................... 1.2 ppm
Hog, fat ........................................................................................... 0.01 ppm
Hog, meat ....................................................................................... 0.01 ppm
Hog, meat byproducts, except liver .............................................. 0.01 ppm
Hog, liver ........................................................................................ 0.15 ppm
Horse, fat ........................................................................................ 0.10 ppm
Horse, meat ..................................................................................... 0.10 ppm
Horse, meat byproducts, except liver ........................................... 0.10 ppm
Horse, liver ...................................................................................... 1.2 ppm
Milk ................................................................................................. 1.2 ppm
Poultry, fat ...................................................................................... 0.05 ppm
Poultry, meat .................................................................................. 0.03 ppm
Poultry, meat byproducts .............................................................. 0.20 ppm
Sheep, fat ........................................................................................ 0.10 ppm

Sheep, meat ........................................................................................ 0.10 ppm
Sheep, meat byproducts, except liver ...................................................... 0.10 ppm
Sheep, liver .......................................................................................... 1.2 ppm

However, due to a subsequent cancer classification of fluopyram by HED CARC, the registrant submitted a letter (Subject: Withdrawal of certain pending new crops for the active ingredient Fluopyram, 8-March-2011) withdrawing tolerance proposals and registration requests for the following crops:

"CG 1B Root veg and 1C Tuberous and corm veg (except potatoes and sugarbeet)
CG2 Leaves of root and tuberous veg
CG3-07A&B Bulb veg
CG4 Leafy veg
CG5 Brassica
CG6A Edible legumes
CG6B Succulent beans and peas
CG6C (part) Dried peas (and some dried beans)
CG7 Foliage of legume veg
CG8 Fruiting veg
CG10 Citrus
CG11 Pome fruit (except apple)
CG13-07A&B Caneberries and Bushberries
CG13-07F Vine fruit (except wine grapes)
CG13-07G Low growing berries (except strawberry)
CG15 Cereal Grains (except for rotational purposes)
CG16 Forage Cereals (except for rotational purposes)
CG17 Grasses grown for forage or seed
CG18 Non grass animal feeds
CG19 Herbs and Spices
CG20 Oilseeds (except canola)
Hops, Globe artichoke, Christmas Trees, Turf and Ornamentals"

In addition, the registant submitted a revised label specifying uses only on the following crops: apple, cucurbit vegetables, dried beans (selected), peanut, potato, stone fruit, sugar beet, strawberry, tree nuts and wine grapes. The revised label reduces the initially proposed seasonal maximum use rates on dried beans, potato, stone fruit, and sugar beet, restricts the use on grapes to wine grapes only, and increases the pre-harvest interval (PHI) for apples to 7-day from the initially proposed PHI of 0 day. The revised label continues to allow crop rotation to alfalfa and cotton, but restricts crop rotation to canola, cereal grains (except rice), and soybean only after application of fluopyram to dried beans and potato. A revised Section F has not been submitted.

In conjunction with this petition, Bayer is requesting registration of Fluopyram 500 SC Fungicide, a 500 g/L (4.16 lb/gal) suspension concentrate (SC; equivalent to a flowable concentrate) formulation [EPA File Symbol No. 264-RNTI].

The registrant withdrew additional pending uses in its letter of 8 August 2011 which states that

**"The crops being withdrawn from these actions are as follows;**
CG9 Cucurbits (except watermelon)

CG12 Stone fruit (except cherry)

**The following crops remain pending for registration**
Potatoes
Sugarbeet
CG6C - Dried beans (select dried beans – see list below*)
Watermelon
Apple
Cherry
Grapes (grown for wine production only)
Strawberry
CG14 Tree nuts (including Pistachio)
Peanuts
CG15 Cereal Grains - for rotational purposes only
CG16 Forage of cereal grains - for rotational purposes only
Canola - for rotational purposes only
Soybean (&forage) - for rotational purposes only
Alfalfa - for rotational purposes only
Cotton - for rotational purposes only
Banana - for import tolerance only

*Dried beans include Dried Shelled Bean, Bean (*Lupinus* spp., includes grain lupin, sweet lupin, white lupin, and white sweet lupin), Bean (*Phaseolus* spp., includes field bean, kidney bean, lima bean (dry), navy bean, pinto bean, tepary bean), Bean (*Vigna* spp., includes adzuki bean, blackeyed pea, catjang, Crowder pea, moth bean, mung bean, rice bean, Southern pea, Urd bean,) Other Beans [Broad bean (dry), chickpea, Guar, Lablab bean, Lentil.]"

The nature of the residue in plants is adequately understood based on metabolism studies with grape, potato, bean, and red pepper. The nature of the residue in rotational crops is adequately understood based on confined rotational crop studies with rotated Swiss chard, turnip, and wheat. The metabolic pathway of fluopyram is similar in primary and rotational crops, and mainly involves hydroxylation of parent compound leading to AE C656948-7-hydroxy and AE C656948-8-hydroxy, conjugation of the hydroxylated parent compound, mainly with sugars, and cleavage of the molecule leading to AE C656948-benzamide, AE C656948-pyridyl-acetic acid (AE C656948-PAA), and AE C656948-pyridyl-carboxylic acid (AE C656948-PCA). HED has determined that the residue of concern in plant commodities (primary and rotational crop) for tolerance enforcement is fluopyram, and for risk assessment is fluopyram in all crops except in legumes and oilseed crops where AE C656948-benzamide is also included (finite levels of the benzamide were only found in beans, peas, rapeseed and rapeseed forage in the EU field trials).

The nature of the residue in livestock is adequately understood based on metabolism studies with goats and hens. Metabolism of fluopyram in livestock mainly involves hydroxylation of the parent compound to AE C656948-7-hydroxy and AE C656948-8-hydroxy, elimination of water from compounds hydroxylated in the ethylene bridge leading to AE C656948-Z/E-olefines, cleavage of the molecule leading to AE C656948-benzamide and AE C656948-PAA, and conjugation of the hydroxylated parent compound, mainly with glucuronic acid. For tolerance enforcement, HED has determined that the residues of concern are fluopyram and AE C656948-benzamide. For risk assessment, the residues of concern in ruminants are fluopyram and its metabolites AE C656948-benzamide, AE C656948-E-olefine, AE C656948-Z-olefine and AE C656948-7-hydroxy, and in hens are fluopyram and its metabolites AE C656948-benzamide, AE C656948-E-olefine, and AE C656948-Z-olefine.

The German multiresidue method DFG Method S 19, a gas chromatography with mass selective detection (GC/MSD) method, has been proposed for the enforcement of tolerances for fluopyram residues in/on crop commodities, and a high performance liquid chromatography (HPLC) method with tandem mass spectrometry detection (MS/MS), Method 01079, has been proposed for the enforcement of tolerances for residues of fluopyram and AE C656948-benzamide in livestock commodities. The validated limit of quantitation (LOQ) is 0.01 ppm for each analyte in each matrix. The proposed enforcement method for plant commodities (DFG Method S19) and livestock commodities (Method 01079) are deemed adequate as enforcement methods. Adequate HPLC/MS/MS methods were used for data collection for crop and livestock commodities. The FDA multiresidue methods of PAM Vol. I are suitable for the determination of fluopyram in non-fatty matrices (using Section 302), but are not suitable for detection of AE C656948-benzamide residues.

Storage stability data have been submitted for residues of fluopyram and metabolites AE C656948-benzamide, AE C656948-PAA, AE C656948-PCA, AE C656948-7-hydroxy, and AE C656948-methyl-sulfoxide (AE 1344122) in/on lettuce, dry pea seed, orange, rape seed, and wheat grain, respectively representing water-, protein-, acid-, oil-, and starch-containing commodities. Under frozen conditions, residues of fluopyram and its metabolite AE C656948-benzamide are stable for at least 36 months in water-, starch-, protein-, oil-, and acid-containing materials, and residues of AE C656948-PCA and AE C656948-methyl-sulfoxide are stable for at least 36 and 24 months, respectively, in protein-, oil-, and acid-containing materials. Residues of AE C656948-PAA are stable for at least 36 months in water-, starch-, protein-, and oil-containing materials, and for 24 months in acid-containing materials. Furthermore, residues of AE C656948-7-hydroxy are stable for at least 36 months in water- and starch-containing materials and for at least 24 months in protein-, oil-, and acid-containing materials.

Based on the livestock metabolism studies which did not show a change in the metabolic profile after 10 months of frozen storage for eggs, muscle and fat of hens and 6 months of frozen storage for milk, fat, kidney and liver of goats, and since the egg, milk, and tissue samples from the livestock feeding studies were stored frozen and analyzed within 30 days of collection, HED concludes that storage stability data for the livestock matrices are unnecessary.

Adequate field trial data are available to support the proposed uses on apple, cucurbit vegetables, dried beans, peanut, potato, stone fruit, strawberry, sugar beet, tree nuts, and wine grapes. Application rates used in the residue field trials conducted on dry beans, cherry, and sugar beet were more than 25% higher than the corresponding proposed maximum seasonal use rates, therefore, the proportionality principle had been applied when estimating the tolerances for these crops using the NAFTA calculator.

The petitioner proposed a tolerance for “nut, tree, group 14 (including pistachio)” at 0.05 ppm. Separate tolerances must be proposed for the tree nut crop group and pistachio. The available data indicate that 0.05 ppm is an appropriate level for these tolerances.

The petitioner has proposed a tolerance and submitted supporting field trial data for banana. The petitioner is not proposing use of fluopyram on banana in the U.S. The petitioner must submit information pertaining to the proposed use of fluopyram on bananas to be imported to the U.S.

Processing studies have been submitted for many crops including apple, canola, field corn, cotton, peanut, plum, potato, soybean, sugar beet, and wheat. The available processing data indicate that tolerances for fluopyram residues are needed for wet apple pomace and processed potato waste. No tolerances are needed for the remaining processed commodities.

Adequate cattle and poultry feeding studies have been submitted. The data indicate that tolerances for livestock commodities (egg, milk, and the fat, meat, and meat byproducts of cattle, goat, hog, horse, poultry, and sheep) are needed to support the proposed fluopyram uses.

The confined rotational crop studies are adequate. An adequate limited field rotational crop study has been submitted. The study indicates the potential for quantifiable fluopyram residues in/on crops rotated 8 months following fluopyram application. Adequate extensive field rotational crop studies with alfalfa and cotton have been submitted to support the proposed 14-day plantback interval (PBI) for these crops, pending one repeat field trial with rotated cotton. The tolerances for alfalfa and cotton commodities must be revised to be specified in terms of indirect or inadvertent residues of fluopyram.

The revised label states "… following potato or dried beans these crops may be planted immediately: canola, cereal grains (except rice), corn and soybean. Do not plant all other crops for one year following the last application." However, extensive field rotational crop data for the specified rotated crops are not available. In the absence of sufficient rotational crop data, the registrant proposed to use the highly conservative target crop residue data for setting rotational crops tolerances. The Chemistry Science Advisory Council (ChemSAC) understands that the selection of an intermediate level between the confined accumulation/ limited field rotational crop data and primary crop data for the target rotated crops would discourage potential misuse (i.e., direct foliar application) and provide adequate maximum residue levels for legal uses according to label instructions (2/9/2011 meeting). Pending extensive field rotational crop data, HED recommends rotational (inadvertent residue) crop tolerances be set at half of the calculated primary crop tolerances with a PBI of 30 days: canola seed at 1.8 ppm, soybean seed at 0.10 ppm, soybean forage at 4.0 ppm, soybean hay at 15 ppm, cereal grains except rice group 15 at 1.5 ppm, and forage at 4.0 ppm, hay at 6.5 ppm, straw at 7.0 ppm, stover at 6.0 ppm of cereal grains except rice group 16.

Since the confined accumulation data reflect a maximum PBI of 280 days when TRRs (total radioactive residues) in some crop matrices still exceed 0.01 ppm, rotation to crops other than those discussed above is not supported. The proposed label should state that crop rotation is prohibited except for the following crops: apple, cherry, dried beans, peanut, potato, sugar beet, strawberry, tree nuts, watermelon, alfalfa, cotton, canola, cereal grains except rice, and soybean.

For harmonization with Codex, the wine grape tolerance should be raised from 1.4 ppm to 2.0 ppm, hog meat byproducts from 0.45 ppm to 0.70 ppm, and milk tolerance from 0.06 ppm to 0.07 ppm.

**Regulatory Recommendations and Residue Chemistry Deficiencies**

HED has examined the residue chemistry database for fluopyram. Pending submission of a revised Section B (see requirements under Directions for Use), a revised Section F (see requirements under Proposed Tolerances), and analytical reference standards (see requirements under Submittal of Analytical Reference Standards), there are no residue chemistry issues that would preclude granting conditional Section 3 registration for the requested uses of fluopyram, or establishment of tolerances for residues of fluopyram. It is recommended that tolerances be established for residues of the fungicide fluopyram (N-[2-[3-chloro-5-(trifluoromethyl)-2-pyridinyl]ethyl]-2-(trifluoromethyl)benzamide), including its metabolites and degradates, in or on the commodities below. Compliance with the tolerance levels specified below is to be determined by measuring only fluopyram in or on the commodity.

| | |
|---|---|
| Almond, hulls | 8.0 ppm |
| Apple | 0.30 ppm |
| Apple, wet pomace | 0.60 ppm |
| Banana | 1.0 ppm |
| Bean, dry | 0.09 ppm |
| Beet, sugar, root | 0.04 ppm |
| Cherry | 0.60 ppm |
| Grape, wine | 2.0 ppm |
| Nut, tree, group 14 | 0.05 ppm |
| Peanut | 0.02 ppm |
| Pistachio | 0.05 ppm |
| Potato | 0.02 ppm |
| Potato, processed potato waste | 0.08 ppm |
| Strawberry | 1.5 ppm |
| Watermelon | 1.0 ppm |

It is recommended that tolerances be established for residues of the fungicide fluopyram (N-[2-[3-chloro-5-(trifluoromethyl)-2-pyridinyl]ethyl]-2-(trifluoromethyl)benzamide), including its metabolites and degradates, in or on the commodities below. Compliance with the tolerance levels specified below is to be determined by measuring only the sum of fluopyram and its metabolite 2-(trifluoromethyl)benzamide, calculated as the stoichiometric equivalent of fluopyram, in or on the commodity.

| | |
|---|---|
| Cattle, fat | 0.11 ppm |
| Cattle, meat | 0.15 ppm |
| Cattle, meat byproducts | 1.1 ppm |
| Egg | 0.25 ppm |
| Goat, fat | 0.11 ppm |
| Goat, meat | 0.15 ppm |
| Goat, meat byproducts | 1.1 ppm |
| Hog, fat | 0.05 ppm |
| Hog, meat | 0.05 ppm |
| Hog, meat byproducts | 0.70 ppm |
| Horse, fat | 0.11 ppm |
| Horse, meat | 0.15 ppm |
| Horse, meat byproducts | 1.1 ppm |
| Milk | 0.07 ppm |
| Poultry, fat | 0.20 ppm |
| Poultry, meat | 0.15 ppm |
| Poultry, meat byproducts | 0.60 ppm |
| Sheep, fat | 0.11 ppm |
| Sheep, meat | 0.15 ppm |

Sheep, meat byproducts....................1.1 ppm

It is recommended that tolerances be established for residues of fungicide fluopyram (N-[2-[3-chloro-5-(trifluoromethyl)-2-pyridinyl]ethyl]-2-(trifluoromethyl)benzamide), including its metabolites and degradates, in or on the commodities below. Compliance with the tolerance levels specified below is to be determined by measuring only fluopyram in or on the commodity.

Alfalfa, forage ....................0.45 ppm
Alfalfa, hay....................1.1 ppm
Canola, seed ....................1.8 ppm
Cotton, gin byproducts ....................0.05 ppm
Cotton, undelinted seed ....................0.01 ppm
Grain, cereal, group 15, except rice....................1.5 ppm
Grain, cereal, forage, fodder and straw, group 16, except rice; forage....................4.0 ppm
Grain, cereal, forage, fodder and straw, group 16, except rice; hay, straw and stover ...........7.0 ppm
Soybean, forage....................4.0 ppm
Soybean, hay ....................15 ppm
Soybean, seed ....................0.10 ppm

The tolerance for banana should include a footnote stating "No U.S. registrations as of [date of FR notice]."

A human health risk assessment is forthcoming.

<u>860.1200 Directions for Use</u>

- The petitioner must submit proposed labels (with English translations if needed) for fluopyram uses on bananas in any countries from which the treated bananas may be imported into the U.S. The available data would support an application pattern of six applications of an SC formulation at 0.100 kg ai/ha/application (0.089 lb ai/A/application) with a 7-day RTI and a 0-day PHI.

- The proposed label must be amended to specify spray application volumes for wine grapes of 50 GPA for ground equipment.

- The proposed labels should be amended to clarify that the unit for application rates is <u>fluid</u> ounces per acre.

- For wine grapes, the proposed label should be amended to include a statement stating that "Do not treat grapes such as Thompson Seedless and Concord which may be used for purposes other than for wine."

- Also, with the exception of the banana field trials and one grape field trial, no spray adjuvants were used in any of the crop field trials. However, HED has recently reviewed bridging field trials conducted on strawberry, grape, cucumber, bulb onion, potato, lettuce, tomato, peach, apple and almond with and without addition of 0.125% v/v of a non-ionic surfactant (Induce®) and concluded that the addition of the NIS had no significant effect on the residue level concentration on these crops. Therefore, the product label must be amended to specify that non-ionic surfactants at 0.125% v/v may be added to spray mixtures.

- The label, under the rotational crop restrictions, must be amended to specify that canola, cereal grains except rice, and soybean may be replanted 30 days following fluopyram application on dry beans and potato only, and that other crops not specified on the label may not be replanted following fluopyram-treated crops.

860.1550 Proposed Tolerances

- The proposed tolerances for the following commodities are too high: reduced tolerances must be proposed: apple wet pomace (0.60 ppm), peanut (0.02 ppm), and processed potato waste (0.08 ppm), sugar beet root (0.04 ppm), and cotton undelinted seed (0.01 ppm).

- Separate tolerances must be proposed for the following commodities: apple (0.30 ppm), cherry (0.60 ppm), dried beans (0.09 ppm), pistachio (0.05 ppm), strawberry (1.5 ppm), and watermelon (1.0 ppm).

- The proposed tolerances for alfalfa and cotton commodities must be revised to be specified in terms of indirect or inadvertent residues of fluopyram. In addition, the proposed tolerances for alfalfa forage and hay must be revised to 0.45 ppm and 1.1 ppm, respectively.

- Separate indirect or inadvertent residues of fluopyram must be proposed for the following commodities: canola, seed (1.8 ppm); grain, cereal, group 15, except rice (1.5 ppm); grain, cereal, forage, fodder and straw, group 16, except rice, forage (4.0 ppm); grain, cereal, forage, fodder and straw, group 16, except rice, hay, straw and stover (7.0 ppm); soybean, seed (0.10 ppm); soybean, forage (4.0 ppm); and soybean, hay (15 ppm).

- Most of the proposed tolerances for livestock commodities are too low. The petitioner must propose increased tolerances as specified in Table 30.

- The proposed tolerances should be revised to reflect the levels and correct commodity definitions as specified in Table 30.

860.1650 Submittal of Analytical Reference Standards

- Analytical reference standard of AE C656948-benzamide must be supplied.

HED recommends that conversion of conditional registration to unconditional registration for the requested uses may be considered upon submission of the following outstanding residue chemistry data.

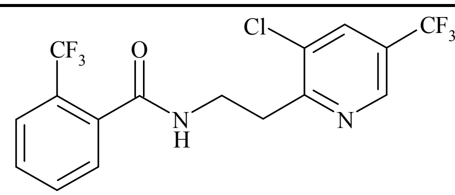
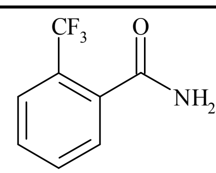
860.1900 Field Accumulation in Rotational Crops

- Submission of the repeat cotton trial due to crop failure, and extensive field rotational crop field trials conducted on canola, cereal grains (except rice), and soybean.

## Background

Fluopyram is a new fungicide with a broad spectrum of activity against numerous fungal diseases in a wide range of crops and plants. Fluopyram represents a new class of chemistry (pyridylethylamide), and its biochemical mode of action has been shown to rely on the inhibition of the enzyme succinate dehydrogenase (complex II) within the fungal mitochondrial respiratory chain, thus blocking electron transport. Fluopyram is a Group 7 fungicide that Bayer initially has proposed for use on the following crops: artichoke (globe); Brassica leafy vegetables; bulb vegetables; canola; cereal grains (except rice); citrus; cucurbit vegetables; fruiting vegetables; ginseng; grapes and small vine fruits (except fuzzy kiwifruit); grasses for forage/feed (including grasses grown for seed); herbs and spices (except black pepper); hops; leafy vegetables; legume vegetables; okra; peanut; pome fruit; potato and other root, tuberous, and corm vegetables; small berries (caneberries and bushberries); stone fruit; strawberry and other low growing berries; sunflower; and tree nuts, including pistachio. Subsequently, the registrant revised the list of crops (as indicated on page 7). The chemical structure and nomenclature of fluopyram are presented in Table 1, and the physicochemical properties of the technical grade of fluopyram are presented in Table 2. This petition represents the first food/feed uses of fluopyram proposed in the U.S. and Canada.

The chemical names and structures of fluopyram metabolites are presented in Appendix I.

| **Table 1. Fluopyram Nomenclature**. | |
|---|---|
| Chemical structure |  |
| Common name | Fluopyram |
| Company experimental name | AE C656948 |
| IUPAC name | *N*-[2-[3-Chloro-5-(trifluoromethyl)-2-pyridyl]ethyl]-α,α,α-trifluoro-*o*-toluamide |
| CAS name | *N*-[2-[3-Chloro-5-(trifluoromethyl)-2-pyridinyl]ethyl]-2-(trifluoromethyl)benzamide |
| CAS registry number | 658066-35-4 |
| End-use product (EP) | Fluopyram 500 SC Fungicide (4.16 lb/gal SC formulation; EPA File Symbol No. 264-RNTI) |
| Chemical structure of AE C656948-benzamide metabolite (included in the tolerance expression for livestock commodities) |  2-(Trifluoromethyl)-benzamide |

| **Table 2. Physicochemical Properties of Fluopyram.** | | |
|---|---|---|
| Parameter | Value | Reference |
| Melting point | 118 ºC | MRID 47372240 |
| pH | 6.6 (1% aqueous solution; pure substance) | MRID 47372236 |
| Density | 1.53 | MRID 47372242 |

| **Table 2. Physicochemical Properties of Fluopyram.** | | |
|---|---|---|
| Parameter | Value | Reference |
| Water solubility (20 °C) | Distilled water (pH 6.7) = 16 mg/L<br>pH 4 = 15 mg/L<br>pH 7 = 16 mg/L<br>pH 9 = 15 mg/L | MRID 47372247 |
| Solvent solubility (g/L at 20 °C) | heptane 0.66<br>toluene 62.2<br>dichloromethane >250<br>methanol >250<br>acetone >250<br>ethyl acetate >250<br>dimethyl sulfoxide >250 | MRID 47372248 |
| Vapor pressure | $1.2 \times 10^{-6}$ Pa at 20 ºC<br>$3.1 \times 10^{-6}$ Pa at 25 ºC<br>$2.9 \times 10^{-4}$ Pa at 50 ºC | MRID 47372249 |
| Dissociation constant ($pK_a$) | 0.5 (23 ºC) | MRID 47372243 |
| Octanol/water partition coefficient Log($K_{OW}$) | 3.3 | MRID 47372245 |
| UV/visible absorption spectrum | Peak max at 270 nm | MRID 47372237 |

## 860.1200 Directions for Use

The petitioner has submitted a draft specimen label for the end-use product containing fluopyram listed in Table 3. The product is an SC formulation. A summary of the proposed use patterns on food and feed crops is detailed in Table 4.

| **Table 3. Summary of Proposed End-Use Products.** | | | | | |
|---|---|---|---|---|---|
| Trade Name | File Symbol No. | ai (% of formulation) | Formulation Type | Target Crops | Label Date |
| Fluopyram 500 SC Fungicide/ LUNA® PRIVILEGE | 264-RNTI | 41.5 [4.16 lb/gal] | SC | Apple, cherry, dried beans, wine grape, peanut, potato, strawberry, sugar beet, tree nuts, and watermelon. | 08/15/11 |

| **Table 4. Summary of Directions for Use of Fluopyram.** | | | | | | |
|---|---|---|---|---|---|---|
| Applic. Timing; Type; and Equipment | Formulation [EPA File Symbol No.] | Applic. Rate (lb ai/A) | Max. No. Applic. per Season | Max. Seasonal Applic. Rate (lb ai/A) | PHI (days) | Use Directions and Limitations[1] |
| **Apple** | | | | | | |
| Postemergence; Foliar spray; Ground, or chemigation | 4.16 lb/gal SC [264-RNTI] | 0.078-0.222 | NS | 0.445 | 7 | The proposed RTI is 7-14 days. |
| **Cherry** | | | | | | |
| Postemergence; Foliar spray; Ground, aerial, or chemigation | 4.16 lb/gal SC [264-RNTI] | 0.092 | NS | 0.183 | 0 | The proposed RTI is 5-7 days. |

| Table 4. Summary of Directions for Use of Fluopyram. | | | | | | |
|---|---|---|---|---|---|---|
| Applic. Timing; Type; and Equipment | Formulation [EPA File Symbol No.] | Applic. Rate (lb ai/A) | Max. No. Applic. per Season | Max. Seasonal Applic. Rate (lb ai/A) | PHI (days) | Use Directions and Limitations[1] |
| **Dried shelled beans**: bean (*Lupinus* spp., includes grain lupin, sweet lupin, white lupin, and white sweet lupin), bean (*Phaseolus* spp., includes field bean, kidney bean, lima bean (dry), navy bean, pinto bean, tepary bean), bean (*Vigna* spp., includes adzuki bean, blackeyed pea, catjang, cowpea, Crowder pea, moth bean, mung bean, rice bean, southern pea, urd bean), other beans (broad bean (dry), chickpea, guar, lablab bean, lentil) | | | | | | |
| Postemergence; Foliar spray; Ground, aerial, or chemigation | 4.16 lb/gal SC [264-RNTI] | 0.134 | NS | 0.268 | 14 | The proposed RTI is 7-14 days. Do not feed hay or threshings or allow livestock to graze in treated areas. |
| **Peanut** | | | | | | |
| Postemergence; Foliar spray; Ground, aerial, or chemigation | 4.16 lb/gal SC [264-RNTI] | 0.182-0.222 | NS | 0.445 | 7 | The proposed RTI is 14 days. Do not feed hay or threshings or allow livestock to graze in treated areas. |
| **Potato** | | | | | | |
| Postemergence; Foliar spray; Ground, aerial, or chemigation | 4.16 lb/gal SC [264-RNTI] | 0.130-0.178 (ground, chemiga-tion) 0.092 (aerial) | NS | 0.356 (ground, chemiga-tion) 0.275 (aerial) | 7 | The proposed RTI is 5-7 days. The grazing of livestock in treated areas within 7 days of application is prohibited. |
| **Strawberry** | | | | | | |
| Postemergence; Drip/ chemigation, greenhouse spray | 4.16 lb/gal SC [264-RNTI] | 0.222 | NS | 0.445 | 0 (drip appli-cation)<br>1 (green-house uses) | The proposed RTI is 5-7 days. Applications may be made to strawberries grown in a greenhouse of 10 acres or larger. |
| **Sugar beet** | | | | | | |
| Postemergence; Foliar spray; Ground, or chemigation | 4.16 lb/gal SC [264-RNTI] | 0.111 | NS | 0.222 | 7 | The proposed RTI is 5-7 days. |
| **Tree nuts:** almond, beech nut, Brazil nut, butternut, cashew, chestnut, chinquapin, filbert (hazelnut), hickory nut, macadamia nut (bush nut), pecan, pistachio, walnut [including black and English (Persian) walnuts] | | | | | | |
| Postemergence; Foliar spray; Ground, aerial, or chemigation | 4.16 lb/gal SC [264-RNTI] | 0.104-0.222 | NS | 0.445 | 14 | The proposed RTI is 7-14 days. |

| Table 4. Summary of Directions for Use of Fluopyram. | | | | | | |
|---|---|---|---|---|---|---|
| Applic. Timing; Type; and Equipment | Formulation [EPA File Symbol No.] | Applic. Rate (lb ai/A) | Max. No. Applic. per Season | Max. Seasonal Applic. Rate (lb ai/A) | PHI (days) | Use Directions and Limitations[1] |
| **Watermelon**: watermelon (includes hybrids and/or varieties of *Citrullus lanatus*) | | | | | | |
| Postemergence; Foliar spray; Ground, or drip/chemigation | 4.16 lb/gal SC [264-RNTI] | 0.078-0.222 | NS | 0.445 | 0 (spray uses)<br>3 (green-house uses)<br>7 (drip appli-cations) | The proposed RTI is 5-14 days. Applications may be made to cucurbits grown in a greenhouse of 10 acres or larger. |
| **Wine Grapes:** varieties only such as but not limited to these varieties: Chardonnay, Cabernet sauvignon, Syrah, Merlot, Pinot Noir, and Zinfandel | | | | | | |
| Postemergence; Foliar spray; Ground, or chemigation | 4.16 lb/gal SC [264-RNTI] | 0.078-0.222 | NS | 0.445 | 7 | The proposed RTI is 12-21 days. |

[1] RTI = Retreatment interval. All applications are to begin preventatively and continue as needed (when multiple applications are permitted).

The label specifies that for field and vegetable crops, applications are to be made in ≥10 GPA for ground equipment and ≥5 GPA for aerial equipment; for tree crops, applications are to be made in ≥50 GPA for ground equipment and ≥15 GPA for aerial equipment. Application volumes for grapes are not specified.

The label specifies that applications may be made as foliar, soil, or soil-less mix applications to cucurbit vegetables and strawberry grown in greenhouse of 10 acres or larger.

The label indicates that the product is compatible with most commonly used fungicides, herbicides, insecticides, and foliar nutrient products. No tank mix partners are specified, but the label recommends that before applying any tank mixture, safety to the crop should be confirmed on a small portion of the crop to be treated.

The label specifies that to limit the potential for development of disease resistance, no more than two sequential applications of fluopyram or any Group 7 fungicide may be made before rotating with a fungicide from a different group.

The following PBIs are specified on the proposed label for EPA File Symbol No. 264-RNTI: 14 days for alfalfa and cotton; and 0 days for apple, cherry, cucurbit vegetables, dried beans, peanut, potato, stone fruit, sugar beet, strawberry, tree nuts, and wine grapes. Furthermore, following potato or dried bean these crops may be planted immediately: canola, cereal grains (except rice), corn and soybean. Do not plant all other crops for one year following the last application.

A 12-hour restricted entry interval (REI) is specified for EPA File Symbol No. 264-RNTI.

*Conclusions*. The use directions are adequate to allow evaluation of the residue data relative to the proposed use in the U.S. The proposed maximum seasonal rate and minimum RTIs are supported by the submitted field trial data. The proposed minimum PHIs are supported by the submitted field trial data.

No North American greenhouse data were submitted. Use of fluopyram on cucurbit vegetables and strawberry grown in a greenhouse is supported by greenhouse data collected in Europe.

No proposed use information was provided for bananas. The petitioner must submit proposed labels (with English translations if needed) for fluopyram uses on bananas in any countries from which the treated bananas may be imported into the U.S. The available data would support an application pattern of six applications of an SC formulation at 0.100 kg ai/ha/application (0.089 lb ai/A/application) with a 7-day RTI and a 0-day PHI.

The proposed label must be amended to specify spray application volumes for wine grapes of 50 GPA for ground equipment. In addition, the proposed labels should be amended to clarify that the unit for application rates is fluid ounces per acre.

For wine grapes, the proposed label should be amended to include a statement stating that “Do not treat grapes such as Thompson Seedless and Concord which may be used for purposes other than for wine.

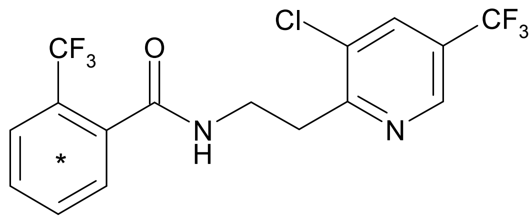
Also, with the exception of the banana field trials and one grape field trial, no spray adjuvants were used in any of the crop field trials. However, HED has recently reviewed bridging field trials conducted on strawberry, grape, cucumber, bulb onion, potato, lettuce, tomato, peach, apple and almond with and without addition of 0.125% v/v of a non-ionic surfactant (Induce®) and concluded that the addition of the NIS had no significant effect on the residue level concentration on these crops. Therefore, the product label must be amended to specify that non-ionic surfactants at 0.125% v/v may be added to spray mixtures.

Adequate data have been submitted to support the proposed PBIs of 14 days for alfalfa and cotton. No extensive field rotational crop data were submitted to support the proposed PBIs of 0 day for canola, cereal grains, and soybean. In the absence of sufficient rotational crop data and based on the foliar crop data, the label must be amended to specify that canola, cereal grains, and soybean may be replanted 30 days following fluopyram application. Based on the confined accumulation and limited field rotational crop data, there is a potential for quantifiable residues of fluopyram in/on rotational crops at PBIs of beyond 12 months. Therefore, all other crops not on the label may not be replanted following fluopyram-treated crops.

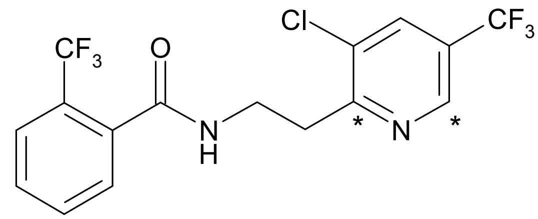
**860.1300 Nature of the Residue - Plants**

First Entry Monograph for Fluopyram, Sections B.7.1.1 through B.7.1.5 (MRIDs 47372524-47372531, and 47372536)

The petitioner submitted studies pertaining to the metabolism of fluopyram in grape, bean, potato, and red pepper. Two different radiolabels were used in the plant studies; the label positions are presented below:




[phenyl-UL-$^{14}$C]AE C656948




[pyridyl-2,6-$^{14}$C]AE C656948

Numerous metabolites were identified in these studies. The chemical structures and report names for these metabolites are provided in Appendix I.

Grape

MRID 47372525: The metabolism was investigated in grape vines following three spray applications with [phenyl-UL-$^{14}$C]fluopyram formulated as a suspension concentrate (SC 500) targeting a maximum annual application rate of 500 g ai/ha. The targeted single application rates amounted to 100 g ai/ha, 200 g ai/ha, and 200 g ai/ha for the first, second, and third application, respectively. The actual total application rate was 504 g ai/ha (0.45 lb ai/A), 1x the proposed maximum seasonal rate to grapes. Applications were performed at growth stages BBCH 17-19, 71, and 81. Grapes and leaves were harvested at maturity with a PHI of 18 days for grapes and 19 days for leaves. After the second application, shoots and leaves ("summer cut") were taken for method development.

The total radioactive residues (TRR) amounted to 28.55 ppm in the summer cut, 1.86 ppm in grapes, and 48.06 ppm in leaves. A total of 98.6% and 93.9% TRR in grapes and leaves, respectively, were extracted conventionally using acetonitrile (ACN)/water.

Parent compound and metabolites in the extracts were quantified by radio-HPLC. A total of 98.6% TRR was identified in grapes and 93.8% TRR in leaves. The TRR consisted nearly quantitatively of unchanged parent compound which represented 1.82 ppm (97.6% TRR) in grapes and 44.11 ppm (91.8% TRR) in leaves. Apart from parent, the residues consisted of AE C656948-benzamide and AE C656948-7-hydroxy in grapes. In the leaves at harvest, AE C656948-7- and 8-hydroxy and the glucoside conjugate of the AE C656948-7-hydroxy were identified.

MRID 47372524: The metabolism was investigated in grape vines following three spray applications with [pyridyl-2,6-$^{14}$C]fluopyram formulated as a suspension concentrate (SC 500) targeting a maximum annual application rate of 500 g ai/ha. The targeted single application rates amounted to 100 g ai/ha, 200 g ai/ha, and 200 g ai/ha for the first, second, and third application, respectively. The actual total application rate was 498 g ai/ha (0.444 lb ai/A), 1x the proposed maximum seasonal rate to grapes. Applications were performed at growth stages BBCH 17-19, 71, and 81. Grapes and leaves were harvested at maturity with a PHI of 18 days for grapes and 19 days for leaves. After the second application, shoots and leaves ("summer cut") were taken for method development.

The TRR amounted to 1.7 ppm for grapes and 42.66 ppm in leaves. A total of 97.1% and 94.7% TRR in grapes and leaves, respectively, were extracted conventionally using ACN/water.

Parent compound and metabolites in the extracts were quantified by radio-HPLC. A total of 97.0% TRR was identified in grapes and 94.7% in leaves. The TRR consisted nearly quantitatively of unchanged parent compound which represented 1.63 ppm (95.8% TRR) in grapes and 39.0 ppm (91.3% TRR) in leaves. Apart from parent, the identified residues consisted of AE C656948-PCA and AE C656948-7-hydroxy in grapes. In the leaves at harvest, the identified residues were AE C656948-7- and 8-hydroxy, the glucoside conjugate of the AE C656948-7-hydroxy and AE C656948-PCA.

Potato

MRID 47372528: The metabolism was investigated in potatoes following three spray applications with [phenyl-UL-$^{14}$C]fluopyram formulated as a suspension concentrate (SC 500). The target application rate for a single application amounted to 167 g ai/ha/application; the actual rates for each of the three applications were 167.3 g ai/ha, 175.6 g ai/ha and 176.0 g ai/ha, resulting in a total actual application rate of 518.8 g ai/ha (0.463 lb ai/A), 1x the proposed maximum seasonal rate to potato. Applications were performed at growth stages BBCH 16, 55, and 71. Potato leaves and tubers were harvested at maturity with a PHI of 51 days.

The TRR for tubers (0.008 ppm) were very low while the TRR in leaves were 47.64 ppm. A total of 96.7% and 99.4% TRR in tubers and leaves, respectively, were extracted conventionally using ACN/water.

Parent compound and metabolites in the extracts were quantified by HPLC. A total of 77.1% TRR was identified in tubers and 99.2% TRR in leaves. Parent compound amounted to 0.006 ppm (68.8% TRR) in tubers and 46.69 ppm (98.0% TRR) in leaves. AE C656948-benzamide (0.001 ppm, 7.1 % TRR) was identified in the extract of tubers by HPLC co-chromatography and also assigned in the extract of leaves (0.23 ppm, 0.5 % TRR). AE C656948-7-hydroxy was detected in low amounts (≤1.2% TRR) in the extracts of tubers and leaves.

MRID 47372529: The metabolism was investigated in potatoes following three spray applications with [pyridyl-2,6-$^{14}$C]fluopyram formulated as a suspension concentrate (SC 500). The target application rate for a single application amounted to 167 g ai/ha/application; the actual rates for each of the three applications were 170.1 g ai/ha, 170.5 g ai/ha and 165.1 g ai/ha, resulting in a total actual application rate of 505.7 g ai/ha (0.451 lb ai/A), 1x the proposed maximum seasonal rate to potato. Applications were performed at growth stages BBCH 16, 55, and 71. Potato leaves and tubers were harvested at maturity with a PHI of 51 days.

The TRR in the tubers (0.012 ppm) were very low while in the leaves TRR were 21.67 ppm. Significant portions of the TRR, 95.3% and 99.6% TRR in tubers and leaves, respectively, were extracted conventionally using ACN/water.

Parent compound and metabolites in the extracts were quantified by HPLC. A total of 74.1% TRR was identified in tubers and 99.2% TRR in leaves. Parent compound amounted to 0.003 ppm (23.2% TRR) in tubers and 21.26 ppm (98.1% TRR) in leaves. AE C656948-PCA was identified in the extract of tubers and leaves at 49.8% TRR (0.006 ppm) and 0.5% TRR (0.11 ppm), respectively. AE C656948-7-hydroxy was detected in low amounts (≤1.1% TRR) in the extracts of tubers and leaves.

Bean

MRID 47372527: The metabolism was investigated in beans following two spray applications with [phenyl-UL-$^{14}$C]fluopyram formulated as a suspension concentrate (SC 500) targeting a maximum annual application rate of 500 g ai/ha (0.446 lb ai/A). The actual rates for each of the two applications were 269 and 259 g ai/ha (0.240 and 0.231 lb ai/A), respectively, resulting in a total actual application rate of about 528 g ai/ha (0.471 lb ai/A), 1x the proposed maximum seasonal rate to legume vegetables. Applications were performed at growth stages BBCH 51 and 75. The immature raw agricultural commodities (RACs) investigated, green beans and foliage, were collected four days after the second application. The mature RACs, beans (succulent shelled bean) and straw, were harvested 29 days after the last application. A portion of the mature beans was dried for 11 days and analyzed as edible RAC dry bean seeds.

The TRR in the edible RACs succulent and dry beans were very low and amounted to 0.07 ppm and 0.12 ppm, respectively. In green beans, foliage, and straw, TRR were 1.40 ppm, 36.66 ppm and 16.55 ppm, respectively. The major amount of radioactivity (93.9-98.1% TRR) was effectively extracted with ACN/water from all RACs.

Parent compound and metabolites in the extracts were quantified by radio-HPLC. The identification rate was high in all RACs and ranged from 84% to 98% TRR.

In the edible RACs succulent and dry beans, the active substance was cleaved to a greater extent compared to the other RACs, green beans, foliage, and straw. In succulent and dry beans, unchanged parent compound represented 11-13% TRR. In these RACs the main metabolite was AE C656948-benzamide which amounted to 0.04 ppm (51.6% TRR) in succulent beans and 0.08 ppm (64.0% TRR) in dry beans.

In green beans, foliage, and straw, the TRR consisted nearly quantitatively of unchanged parent compound which represented >90% TRR. AE C656948-benzamide was either not detected or represented <1% TRR in these RACs.

Apart from the active substance and AE C656948-benzamide, AE C656948-7-hydroxy, AE C656948-8-hydroxy, and several conjugates of the hydroxylated active substance were identified.

MRID 47372526: The metabolism was investigated in beans following two spray applications with [pyridyl-2,6-$^{14}$C]fluopyram formulated as a suspension concentrate (SC 500) targeting a maximum annual application rate of 500 g ai/ha (0.446 lb ai/A). The actual rates for each of the two applications were 265 and 254 g ai/ha (0.236 and 0.227 lb ai/A), respectively, resulting in a total actual application rate of about 519 g ai/ha (0.463 lb ai/A), 1x the proposed maximum seasonal rate to legume vegetables. Applications were performed at growth stages BBCH 51 and 75. The immature RACs, green beans and foliage, were collected four days after the second application. The mature RACs, beans (succulent shelled bean) and straw, were harvested 29 days after the last application. A portion of the mature beans was dried for 11 days and analyzed as edible RAC dry bean seeds.

The TRR in the edible RACs succulent and dry beans were very low and amounted to 0.17 ppm and 0.31 ppm, respectively. In green beans, foliage and straw, TRR amounted to 3.88 ppm, 38.53 ppm, and 19.02 ppm, respectively. The major amount of radioactivity (95.7-99.3% TRR) was effectively extracted with ACN/water from all RACs.

Parent compound and metabolites in the extracts were quantified by radio-HPLC. A total of 76% to 99% TRR was identified in the RACs.

In the edible RACs succulent and dry beans, the active substance was cleaved to a greater extent compared to the other RACs, green beans, foliage, and straw. In succulent and dry beans, unchanged parent compound represented 4.8-5.7% TRR. In these RACs, AE C656948-PAA and AE C656948-PCA were the main metabolites representing 23-33% TRR. A third and minor label-specific metabolite, AE C656948-hydroxyethyl-glycoside, was detected and represented ≤3.1% TRR.

In green beans, the TRR consisted quantitatively of unchanged parent compound which represented 99.3% TRR. In foliage, parent compound amounted to 92.3% TRR and 6 minor metabolites were identified. In straw, parent compound amounted to 87.1% TRR and 7 minor metabolites were identified.

Apart from the active substance and the three label-specific metabolites, AE C656948-7-hydroxy, AE C656948-8-hydroxy, and several conjugates of the hydroxylated active substance were identified.

Red pepper

MRID 47372531: The metabolism of the fungicide fluopyram was investigated in red bell pepper following drip irrigation with [phenyl-UL-$^{14}$C]fluopyram formulated as a suspension concentrate (SC 500). An aqueous dilution of the formulation was applied to the plants growing on stone wool substrate according to practice in professional horticulture. The targeted single application rate amounted to 5 mg ai/plant. Additionally, an overdose experiment (4x) was conducted at 20 mg ai/plant for method development and to facilitate identification of metabolites. The applications were performed when the fifth to seventh leaf of the main shoot was unfolded (BBCH 15-17).

A plant at an intermediate growth stage was harvested from the 4x experiment 33 days after application. Fruits were harvested at maturity from plants of the 1x experiment at three time points (55-96 days after application). The remaining plants were sampled one day after the third harvest of fruits (97 days after application). The RACs from the overdose experiment were used to facilitate isolation and identification of metabolites.

The TRR in the mature fruits were very low and amounted to 0.038 ppm. In the rest of the plant, TRR amounted to 3.54 ppm. The major amount of radioactivity (>96% TRR) was effectively extracted with ACN/water from all RACs.

Parent compound was the major part of the residue in the fruits and the rest of the plant (48.9% and 64.0% TRR, respectively). The main metabolite was the cleavage product AE C656948-benzamide (16.1% TRR in fruits and 10.0% TRR in remaining plants). Other metabolites detected (≤9% TRR each) were AE C656948-7-hydroxy and its glucoside conjugate in both fruits and the remaining plants. In the rest of the plant, AE C656948-8-hydroxy and a malonic acid conjugate of the AE C656948-7-hydroxy-glc were additionally observed at minor amounts (<1% TRR each).

MRID 47372530: The metabolism of the fungicide fluopyram was investigated in red bell pepper following drip irrigation with [pyridyl-2,6-$^{14}$C]fluopyram formulated as a suspension concentrate (SC 500). An aqueous dilution of the formulation was applied to the plants growing on stone wool substrate according to practice in professional horticulture. The targeted single application rate amounted to 5 mg ai/plant. Additionally, an overdose experiment (4x) was conducted at 20 mg ai/plant for method development and to facilitate identification of metabolites. The applications were performed when the fifth to seventh leaf of the main shoot was unfolded (BBCH 15-17).

A plant at an intermediate growth stage was harvested from the 4x experiment 33 days after application at BBCH 61. Fruits were harvested at maturity from plants of the 1x and the 4x experiment at three time points (55-96 days after application). The remaining plants were sampled one day after the third harvest of fruits (97 days after application).

The TRR in the mature fruits (1x) were very low and amounted to 0.06 ppm. In the rest of the plant, TRR amounted to 2.34 ppm. The major amount of radioactivity (>95% TRR) was effectively extracted with ACN/water from all RACs.

In the fruits parent compound amounted to 0.01 ppm (16.2% TRR). Identified metabolites were the cleavage product AE C656948-PCA and two glycoside isomers of the AE C656948-PAA amounting to 0.026 ppm (43.5% TRR), 0.014 ppm (23.8% TRR) and 0.009 ppm (14.2% TRR), respectively. Non-conjugated AE C656948-PAA and AE C656948-7-hydroxy were additionally found in the fruits of the 4x overdose experiments.

In the rest of the plant (1x), parent compound accounted for the major part of the residues (1.64 ppm, 70.1% TRR). Only minor metabolites were detectable (each ≤9.2% TRR) and consisted of AE C656948-7-hydroxy and its glucose conjugate, AE C656948-N-oxide, and a higher glucose conjugate of the cleavage product AE C656948-hydroxyethyl. In the intermediate plant (4x), AE C656948-8-hydroxy was additionally identified.

Additional studies

The petitioner submitted a study of the degradation of fluopyram in plant suspension cell cultures. The main purpose of this study was to facilitate metabolite identification and to produce radiolabeled reference compounds for the identification of metabolites in the plant and livestock metabolism studies. Radiolabeled reference standards of the following compounds were generated in the cell culture study: AE C656948-deschloro-3-OH-glc; AE C656948-7-hydroxy; AE C656948-7-hydroxy-glc; AE C656948-8-hydroxy-glc; AE C656948-hydroxymethyl-benzamide; AE C656948-benzamide; AE C656948-pyridyl-hydroxyethyl; AE C656948-pyridyl-hydroxymethyl; and AE C656948-PCA.

The petitioner also noted that the metabolism of fluopyram in cereal grains after seed treatment was not investigated in a separate metabolism study; the petitioner stated that seed treatment use of fluopyram on cereal grains will be proposed in Europe. The petitioner concluded that data on the metabolism of fluopyram in cereals following uptake from the soil, from the first rotation of the confined rotational crop studies (see 860.1850), would be equivalent to seed treatment. The petitioner stated that the highest seed treatment rate in cereals will be 1 g ai/dt [1 g ai/100 kg], equivalent to a worst case application rate of 2.4 g ai/ha (0.0021 lb ai/A). The application rate used in the confined rotational crop studies was 500 g ai/ha (~200x the seed treatment equivalent rate). In contrast to the situation of seed treatment, the test substance in the rotational crop studies was evenly applied to the bare ground, and wheat seeds were planted 30 days following application. The petitioner stated that the results from the laboratory aerobic soil degradation studies with radiolabeled fluopyram show that after 30 days, 81-92% of the applied active substance is still available in soil (i.e., at least 405 g ai/ha from application at 500 g ai/ha).

*Conclusions*. The submitted plant metabolism studies are adequate. The results of the submitted studies with grape, potato, bean, and red pepper indicate that the metabolism of fluopyram is similar in these crops. The metabolism of fluopyram in plants appears to proceed via hydroxylation of parent compound leading to AE C656948-7-hydroxy and AE C656948-8-hydroxy, conjugation of the hydroxylated parent compound mainly with sugars, and cleavage of the molecule leading to AE C656948-benzamide, AE C656948-PAA, and AE C656948-PCA. Further conjugation of AE C656948-7-hydroxy-glucose with malonic acid was observed in bean and red pepper; in addition, cleavage of the molecule yielded glycoside conjugates and AE C656948-hydroxyethyl conjugates in bean and red pepper.

The submitted studies are adequate to satisfy plant metabolism data requirements. The submitted studies represent three dissimilar crop types (fruit/fruiting vegetable, root crop, and a pulse/oil seed), and the parent was found to be the major residue in all four studies. The residue of concern in plant commodities for tolerance enforcement is fluopyram; the residue of concern in plant commodities except in legumes and oilseed crops for risk assessment is fluopyram, and in legumes and oilseed crops is fluopyram plus C656948-benzamide (ROCKS decision memo, 7/16/2009).

**860.1300 Nature of the Residue - Livestock**

First Entry Monograph for Fluopyram, Sections B.7.2.1 and B.7.2.2 (MRIDs 47372532-47372535)

There are several livestock feedstuffs associated with the proposed uses of fluopyram. The petitioner provided livestock metabolism studies with lactating goats and laying hens, which are summarized below.

<u>Hen</u>

<u>MRID 47372532</u>: In a metabolism study with [phenyl-UL-$^{14}$C]AE C656948, six hens were orally dosed for 14 consecutive days in 24 h intervals with 2.03 mg per kg body weight per day (corresponding to 26.42 mg ai/kg feed) and sacrificed about 24 hours after the last dose. The dosing level corresponds to ~21x the estimated dietary burden of fluopyram to poultry (see Table 8). The dose was tolerated without any observable toxicological sign. Total radioactivity was measured in the excreta and eggs, which were collected daily, as well as in the dissected tissues muscle, fat, liver, and skin collected at sacrifice. The eggs, muscle, fat, liver, and excreta were analyzed for parent compound and metabolites.

The overall recovery (sum of radioactivity in the excreta, eggs as well as organs and tissues) was 94.8% of the total administered dose. The majority of the radioactivity (82.7% of the total dose) was detected in the excreta collected before sacrifice. The excretion was high and started immediately after the first administration; the time course of the excretion was characterized by a relatively constant rate starting at Day 2 until test end. Radioactivity in eggs accounted for 4.3% of the total dose. At sacrifice, the compound-related residues in the edible organs and tissues dissected from the bodies amounted to 7.8% of the total dose. From this, more than half (4.9%) was detected in the muscle.

The TRR values in eggs ranged from 0.462 (Day 1) to 3.901 ppm (Day 14). An approximately linear increase was observed until Day 7 (3.243 ppm). After that the residues increased slightly to the test end; however, residues had not plateaued by the end of the dosing period. The TRR in the eggs collected from the ovary and oviduct (5.771 ppm) were 1.5x the TRR in laid eggs at the test end (3.901 ppm). TRR were highest in liver (9.536 ppm) and kidney (5.759 ppm), and lower in muscle (3.290 ppm), skin (2.533 ppm), and subcutaneous fat (1.696 ppm).

For analysis of parent compound and metabolites, Day 1-6 and Day 7-14 eggs, muscle, fat, liver, and Day 14 excreta samples from all animals were respectively pooled, and the pooled samples were extracted with ACN/water. After solid-phase extraction (SPE) purification, the resulting extracts of eggs, muscle, fat, liver, and excreta represented between ca. 92% and 99% TRR in the sample.

The major component in all the edible matrices was the metabolite AE C656948-benzamide, at 68.6% to 98.6% TRR. Other metabolites identified were AE C656948-Z-olefine (25.9% TRR in fat and ≤1.2% TRR in egg, muscle, and liver), AE C656948-E-olefine (≤2.3% TRR in fat and liver), and AE C656948-benzoic acid (0.3% TRR, in liver only). Parent compound was detected as a minor component only in eggs and fat at ≤2.5% TRR. Identification rates in the organs and tissues ranged from 93% to 99% TRR.

<u>MRID 47372533</u>: In a metabolism study with [pyridyl-2,6-$^{14}$C]AE C656948, six hens were orally dosed for 14 consecutive days in 24 h intervals with 2.02 mg per kg body weight per day (corresponding to 25.96 mg ai/kg feed) and sacrificed about 24 hours after the last dose. The dosing level corresponds to ~21x the estimated dietary burden of fluopyram to poultry (see Table 8). The dose was tolerated without any observable toxicological sign. Total radioactivity was measured in the excreta and eggs daily, as well as in the dissected tissues muscle, fat, liver, and skin at sacrifice. The eggs, muscle, fat, liver, and excreta were analyzed for parent compound and metabolites.

The overall recovery (sum of radioactivity in the excreta, eggs as well as organs and tissues) was 95.6% of the total administered dose. The majority of the radioactivity (94.7% of the total dose) was detected in the excreta collected before sacrifice. The excretion rate was high and started immediately after the first administration; the time course of the excretion was characterized by a relatively constant rate starting at Day 2 until test end. Radioactivity in eggs accounted for 0.4% of the total dose. At sacrifice, the compound-related residues in the edible organs and tissues collected from the hens amounted to 0.5% of the total dose.

The TRR in eggs ranged from 0.047 (Day 1) to 0.321 ppm (Day 8). A linear increase was observed until Day 8; after that the residues decreased slightly to 0.262 ppm (Days 13 and 14), and the residue plateau was reached. The TRR in the eggs collected from the ovary and oviduct at sacrifice (0.831 ppm) were about 3x the TRR in laid eggs at the test end (0.262 ppm). The TRR were 0.538 ppm in liver, 0.242 ppm in kidney, 0.498 ppm in subcutaneous fat, 0.152 ppm in skin, and 0.048 ppm in muscle.

For analysis of parent compound and metabolites, Day 1-6 and Day 7-14 eggs, muscle, fat, liver, and Day 14 excreta samples from all animals were respectively pooled, and the pooled samples were extracted with ACN and/or ACN/water (eggs, muscle, liver, and excreta) or with ACN/water and heptane (fat). After SPE purification, the resulting extracts of eggs, muscle, fat, liver, and excreta represented 43-54%, 58%, 99%, 32% and 92%, respectively, of the TRR. Alternatively, egg pools and liver were extracted after enzymatic digestion to try to solubilize more of the radioactive residues; 64-66% in eggs and 82% in liver was recovered after SPE cleanup of the extract. Residual solids in egg pool Day 7-14 following conventional extraction and in liver following enzymatic extraction were exhaustively extracted using microwave extraction releasing an additional 51.2% and 7.4% TRR, respectively. In these samples, remaining nonextractable residues were 1% and 9.7% TRR. Nonextractable residues in muscle and fat were <0.05 ppm.

The major component identified was the metabolite AE C656948-Z-olefine which accounted for 15.4-19.3% TRR in eggs Day 7-14, 33.0% TRR in muscle, and 70.5% TRR in the fat, but only 4.1% TRR in eggs Day 1-6, and 1.9-3.1% TRR in liver. The other isomer AE C656948-E-olefine was found at 11.8-13.9% TRR in fat and liver, and 1.0-3.9% TRR in eggs and muscle. Parent compound was a major residue identified in eggs Day 1-6 at 14.7-17.9% TRR and 12.2% TRR in fat; the parent was identified as a minor residue (≤9.5% TRR) in eggs Day 7-14 and muscle, and was not detected in liver. AE C656948-PAA and AE C656948-7-hydroxy were only minor metabolites, each present at ≤6.4% TRR in eggs and liver. The absolute levels of the individual metabolites common for both labels (phenyl and pyridyl) were very similar in this study to the levels measured after dosing of [phenyl-UL-$^{14}$C]AE C656948. Identification rates in the eggs, organs, and tissues ranged from 20% to 95% TRR.

Due to a high amount of matrix components and the low concentration of radioactivity, no HPLC profile of the microwave extracts, which represented 51.2% TRR (0.146 ppm) in eggs and 7.4% TRR (0.039 ppm) in liver, could be recorded. However, the profile of the egg extract after enzymatic digestion showed neither significant amounts of further metabolites nor different amounts of metabolites compared to the profile of the conventional extract. Based on this result, the petitioner proposed that the radioactivity released by microwave extraction from the solids did not consist of any further unknown metabolites.

*Conclusions - Hen*. The submitted phenyl-label hen metabolism study is adequate. When considered on its own, the pyridyl-label hen metabolism study is not adequate to satisfy data requirements. Fat was the only matrix for which the majority of the radioactivity was identified (95% TRR); less than 40% TRR was identified in eggs, muscle, and liver. TRR in the pooled eggs and tissues were at most a quarter of the activity levels found in the phenyl-label study.

However, in consideration of the pyridyl-label study and the phenyl-label study together, HED concludes that adequate hen metabolism data have been submitted. Based on TRR levels, radioactivity resulting from the pyridyl portion of fluopyram accounted for much less in hen matrices than radioactivity resulting from the phenyl portion, and ≥93% TRR was identified in hen matrices in the phenyl-label study. A larger amount of the dosed radioactivity was excreted in the pyridyl-label study (94.7%) than in the phenyl-label study (82.7%). In addition, the absolute ppm levels of metabolites that were detected in both studies (parent and the olefines) were very similar.

The most important metabolic reaction in the laying hen was the cleavage of the aliphatic chain, yielding the major metabolite AE C656948-benzamide. A second major metabolic reaction involved the hydroxylation of the aliphatic chain followed by elimination, yielding the olefines.

Hydrolysis of the amide to the parent carboxylic acid, AE C656948-benzoic acid, and oxidative cleavage of the aliphatic chain, yielding AE C656948-PAA, were observed as minor reactions.

Goat

MRID 47372535: A goat was orally dosed for five consecutive days, at 24 h intervals, with 1.91 mg [phenyl-UL-$^{14}$C]fluopyram per kg body weight per day (corresponding to 46.26 mg ai/kg feed) and sacrificed at about 24 hours after the last dose. The dosing level corresponds to ~24x the estimated dietary burden of fluopyram to beef cattle and ~14x the dietary burden to dairy cattle (see Table 8). Total radioactivity was measured in milk (collected each morning prior to dosing and 8 hours later in the evening), plasma, and excreta at timed sampling intervals, and in the edible organs and tissues liver, kidney, muscle, and fat collected at sacrifice. The milk (pooled am and pm samples), edible organs and tissues, and excreta (urine and feces) were analyzed for parent compound and metabolites.

The overall recovery (sum of radioactivity in the excreta, milk as well as organs and tissues) was 93.5% of the total administered dose. Up to the time of sacrifice, the excretion accounted for about 88.3% of the total dose, with 52.6% in the urine and 35.7% in the feces. The cumulative urinary and fecal excretion rate was characterized by a linear increase during the whole testing period.

The TRR in plasma, determined over the whole testing period in timed sampling intervals, increased continuously until the test end. During the 8-hour period after each dosing, a very significant increase was observed. In the following 16-hour time range until delivery of the next dose, the TRR values increased or decreased only slightly. This indicated an ongoing absorption of the test item, a rapid distribution of the systemically bioavailable compound-related radioactivity within the body, and a delayed excretion. A plateau level of plasma concentration was not reached during the observation period.

The time course of TRR in milk samples collected 8 hours (evening milk) and 24 hours (morning milk) after each dosing was similar to that of plasma. The radioactive residues increased continuously until the test end by a factor of 10 in total; residues did not reach a plateau in milk during the study period. The TRR in milk samples ranged from 0.045 to 0.454 ppm, and the highest value was detected just before sacrifice. Pooled samples of morning milk (TRR: 0.276 ppm) and evening milk (TRR: 0.228 ppm) were extracted for metabolism investigations.

In tissues, TRR were highest in liver, at 8.379 ppm. The TRR for the other organs and tissues, in decreasing order, were 2.295 ppm in kidney, 0.737 ppm in muscle, and 0.399 ppm in fat. In total, the compound-related residues in all samples were calculated to be about 4.6% of the total dose.

Radioactivity was extracted efficiently (97% to 99% TRR) from milk and fat using conventional solvent extraction. For muscle, liver, and kidney, 68-77% TRR was extracted using conventional solvent extraction; an additional exhaustive extraction step with microwave assistance at increased temperature was used to solubilize an additional 17-32% TRR from these tissues. Nonextractable residues were ≤6% TRR in all goat matrices.

The major component in all the edible matrices was the metabolite AE C656948-benzamide (49.1% to 97.6% TRR). Other major compounds identified were AE C656948-Z-olefine and the parent compound, which were found at 13.1% and 18.2% TRR, respectively, in fat. AE C656948-Z-olefine was identified as a minor residue (<1% TRR) in milk and liver and was not found in muscle and kidney. The parent compound was identified as a minor component in milk, liver, and kidney, at ≤1.7% TRR, and was not detected in muscle. The following additional metabolites were identified as minor residues (<9% TRR each) in goat matrices: AE C656948-benzamide-SA, AE C656948-7-OH-GA (isomers 1 and 2), AE C656948-di-OH-GA (kidney only), AE C656948-phenol-GA (liver and kidney only), AE C656948-8-OH-GA (isomer 2; liver and kidney only), AE C656948-7-hydroxy, and AE C656948-E-olefine (fat and liver only). Identification rates in milk and tissues ranged 93.5-98.9% TRR.

MRID 47372534: A goat was orally dosed for five consecutive days, in 24 h intervals, with 2.0 mg [pyridyl-2,6-$^{14}$C]fluopyram per kg body weight per day (corresponding to 44.62 mg ai/kg feed) and sacrificed at about 24 hours after the last dose. The dosing level corresponds to ~23x the estimated dietary burden of fluopyram to beef cattle and ~13x the dietary burden to dairy cattle (see Table 8). Total radioactivity was measured in milk (collected each morning prior to dosing and 8 hours later in the evening), plasma, and excreta at timed sampling intervals, and in the edible organs and tissues liver, kidney, muscle, and fat collected at sacrifice. The milk (pooled evening samples), edible organs and tissues, and excreta (urine and feces) were analyzed for parent compound and metabolites.

The overall recovery (sum of radioactivity in the excreta, milk as well as organs and tissues) was 81.9% of the total administered dose. Up to the time of sacrifice, the excretion accounted for 81.0% of the total dose, with 52.3% found in the urine and 28.6% in the feces. The cumulative urinary and fecal excretion rate was characterized by a linear increase during the whole testing period.

The TRR in plasma, determined over the whole testing period in timed sampling intervals followed a diurnal course. During the 8-hour period after each dosing, a significant increase was obtained followed by a decrease measured prior to the delivery of the next dose. This indicated rapid absorption of the test item, rapid internal distribution of the systemically bioavailable compound-related radioactivity, and rapid elimination from the body. The radioactive residues in plasma reached a plateau level at about 50-60 hours after the first dosing.

The time course of TRR in the evening and morning milk samples after each dosing showed a similar diurnal pattern as the plasma. The radioactive residues increased significantly during the 8-hour period after each dosing followed by a decrease measured prior to the delivery of the next dose. The TRR in milk reached a plateau at about 32 hours after the first dosing.
The TRR in milk ranged from 0.017 to 0.063 ppm; the highest value was detected at 32 h after the first dose followed by a decrease to 0.026 ppm at sacrifice. Pooled samples of evening milk (TRR: 0.053 ppm) were extracted for metabolism investigations.

In tissues, TRR were highest in liver, at 1.427 ppm. The TRR for the other organs and tissues, in decreasing order, were 0.403 ppm in kidney, 0.372 ppm in fat, and 0.042 ppm in muscle.

Radioactivity was extracted efficiently (89% to 97% TRR) from milk (pooled evening samples), muscle, fat and kidneys by conventional solvent extraction and more than 85% TRR from each of these matrices was analyzed for metabolic profiling. For liver, only 55% TRR was released with conventional solvent extraction; an additional 6.5% TRR was released with further solvent extraction with ACN/aqueous $NH_3$. An additional exhaustive extraction step with microwave assistance at increased temperature was needed for solubilization of residual radioactivity in liver which remained in the solids after conventional solvent extraction; microwave extraction released 15% TRR. Even after this extraction step, only 76% TRR in the liver was extracted; approximately 65% TRR was analyzed by chromatography. Nonextractable residues were ≤0.035 ppm (2.9-10.8% TRR) in all goat matrices except liver. In liver, nonextractable residues were 24.2% TRR (0.346 ppm) following microwave extraction. Although additional microwave extraction of liver solids with ACN/aqueous $NH_3$ solubilized all of the residues, the extracts could not be chromatographically analyzed due to low radioactivity in the fractions or because of matrix interference.

The parent compound was identified as a major component in milk, muscle, and fat (27.3-46.4% TRR) but was only found as a minor residue in liver (7.7% TRR) and was not found in kidney. The metabolite AE C656948-Z-olefine was identified as a major metabolite in milk, muscle, and fat, at 12.9-33.7% TRR; it was found at 5.7% TRR in liver and was not found in kidney. The other isomer AE C656948-E-olefine was found at <5% TRR in milk, muscle, fat, and liver. AE C656948-7-hydroxy was also found to be a major component of milk, muscle, and fat, at 12.8-21.6% TRR, but a minor residue (≤6% TRR) in liver and kidney. Other major identified metabolites included AE C656948-7-OH-GA (isomer 1), at 24.2-35.1% TRR in liver and kidney; AE C656948-7-OH-GA (isomer 2), at 16.3% TRR in kidney; and AE C656948-8-OH-GA (isomer 2) at 17.7% TRR in kidney. These metabolites were also found at <10% TRR in milk, muscle, and liver. AE C656948-PAA, AE C656948-hydroxyethyl-GA, AE C656948-di-OH-GA, and AE C656948-phenol-GA were only minor metabolites, each present at ≤8.6% TRR in liver and kidney.

*Conclusions - Goat*. The submitted goat metabolism studies are adequate to satisfy data requirements. Based on the results of these studies, the petitioner concluded that the metabolism of fluopyram in goats proceeds via the following reactions:

- hydroxylation of the ethylene bridge of the molecule resulting in AE C656948-7-hydroxy, AE C656948-8-hydroxy, and a dihydroxylated compound;
- hydroxylation of the phenyl ring leading to AE C656948-phenol;
- conjugation of the hydroxylated metabolites with glucuronic acid;
- elimination of water from compounds hydroxylated in the ethylene bridge leading to AE C656948-Z-olefine and AE C656948-E-olefine (E- and Z-olefine can isomerize into each other);
- cleavage of the aliphatic chain to form AE C656948-benzamide and AE C656948-pyridyl-hydroxyethyl;
- hydroxylation of AE C656948-benzamide followed by conjugation with sulfate;
- conjugation of AE C656948-pyridyl-hydroxyethyl with glucuronic acid;
- and oxidation of AE C656948-pyridyl-hydroxyethyl to AE C656948-PAA.

*Overall Conclusions - Livestock Metabolism.* The nature of the residue in livestock is adequately understood. The metabolism of fluopyram in poultry and ruminants was found to be similar. The residues of concern for tolerance enforcement are fluopyram and AE C656948-benzamide, and the residues of concern for risk assessment are fluopyram and its metabolites AE C656948-benzamide, AE C656948-E-olefine, and AE C656948-Z-olefine (ROCKS decision memo, 7/16/2009).

**860.1340 Residue Analytical Methods**

A summary of the analytical methods associated with this petition is presented in Table 5.

| **Table 5. Summary of Residue Analytical Methods.** | | | | |
|---|---|---|---|---|
| Matrix | Analyte | Method No. | Method principle | LOQ (fluopyram equivalents) |
| **Crop commodity data generation methods Europe** | | | | |
| Crop commodities from storage stability study; bell pepper, tomato, cucumber, melon, and strawberry samples from greenhouse studies | AE C656948<br>- benzamide<br>- PCA<br>- PAA[2]<br>- 7-hydroxy<br>- methyl-sulfoxide | 00984 | HPLC/MS/MS[1] | 0.01 ppm for all substances, excepted for cereal straw (0.05 ppm) |
| Processed commodities of apple, grape, strawberry, rape seed and tomato | AE C656948<br>- benzamide<br>- PCA<br>- PAA[2] | 00984/M001 | HPLC/MS/MS[1] | 0.01 ppm for all substances |
| **Crop commodity data generation method North America** | | | | |
| All crop commodities from U.S./Canada crop field trial, processing, and field rotational crop studies | AE C656948 | GM-001-P07-01 Modification of method 00984 | HPLC/MS/MS[1] | 0.01 ppm |
| **Crop commodity enforcement method + ILV** | | | | |
| Validated using lettuce, head; oilseed rape, seeds; wheat, grain; orange, fruit; and peas, seed | AE C656948 | S 19<br>DFG method | GC/MSD[3] | 0.01 ppm |
| Validated using oilseed rape, seeds; wheat, grain; orange, fruit; and cabbage, head | AE C656948 | ILV<br>DFG method S 19 | GC/MSD[3] | 0.01 ppm |
| **Livestock commodity data generation method** | | | | |
| Cattle and hen feeding studies | AE C656948<br>- benzamide<br>- olefine (E-isomer)[4]<br>- olefine (Z-isomer)[4] | 01061 | HPLC/MS/MS[1] | - 0.01 ppm for fluopyram and benzamide<br><br>- 0.02 ppm for the two olefines[4] |
| **Livestock commodity enforcement method + ILV** | | | | |
| Validated using cattle milk, liver, fat, muscle, and kidney; and hen whole egg | AE C656948<br>- benzamide | 01079 | HPLC/MS/MS | 0.01 ppm for all substances |

| **Table 5.** **Summary of Residue Analytical Methods.** | | | | |
|---|---|---|---|---|
| Matrix | Analyte | Method No. | Method principle | LOQ (fluopyram equivalents) |
| Validated using cattle milk, liver, and muscle; and hen whole egg | AE C656948 - benzamide | ILV of method 01079 | HPLC/MS/MS | 0.01 ppm for all substances |
| **Multi-residue method** | | | | |
| PAM Multiresidue Analysis | AE C656948 - benzamide | PAM: E1 extraction and DG17 detection without Florisil cleanup | GC | |

1 Two different MRM transitions were measured each time.
2 AE C656948-PAA sodium salt injected.
3 Three ions were monitored in parallel (m/z 223, 173, 396).
4 There was inter-conversion between the E and Z isomers of AE C656948-olefine during analysis. Following fortification with one isomer, both isomers could be separated and determined. The amount of inter-conversion is dependent on various factors (such as matrix and concentration); therefore, a total recovery (summing both olefins) was calculated and reported.

## Crop commodities

First Entry Monograph for Fluopyram, Section B.5.2.1 (MRIDs 47372603, 47372537-47372539, 47372543-47372547)

Bayer has proposed the German multiresidue method DFG Method S 19, for the enforcement of tolerances for fluopyram residues in/on crop commodities. The method was validated using samples of orange (fruit), oil seed rape (seeds), wheat (grain), lettuce (head) and dry peas (seeds). The method was not used for analysis in any of the storage stability, crop field trial, processing, or field rotational crop studies submitted with this petition.

DFG Method S 19: The extraction of fluopyram from orange (fruit) was performed according to extraction module E 3, extraction module E 2 was used for wheat (grain) and dry peas (seeds), extraction module E 7 was used for oil seed rape (seeds), and extraction module E 1 was used for lettuce (head). Briefly, samples other than oil seeds are mixed with water and then the mixture is extracted with acetone and ethyl acetate:cyclohexane (1:1, v:v). Oil seeds are extracted with a mixture of acetone and ACN, and the extract is concentrated and redissolved in ethyl acetate:cyclohexane (1:1, v:v). The organic phase is then cleaned up using module GPC (gel permeation chromatography); the eluate is concentrated and redissolved in ethyl acetate for analysis. All specimens are analyzed by GC/MSD. The ions 223, 173 and 396 (used for quantitation) were used in the validation for the determination of fluopyram using GC/MSD. Quantification was achieved with external standards.

For fluopyram in orange fruit, rape seeds, wheat grain, lettuce (head), and dry pea seeds, the LOQ was 0.01 ppm, and the calculated limit of detection (LOD) was 0.003 ppm. Analysis of control specimens of orange fruit, rape seeds, wheat grain, lettuce, and dry peas seeds by GC/MSD yielded no residues of fluopyram above the LOD (i.e. 0.003 ppm), indicating that no background level of fluopyram was present in the test system of the study.

The method was adequately validated in orange fruit, rape seed, wheat grain, lettuce, and dry pea seeds at fortification levels of 0.01 and 0.10 ppm. The average recoveries were within acceptable limits (70-120%), and relative standard deviations (RSDs) were <20% for each fortification level, matrix, and analyte. Recoveries of fluopyram ranged 68-111% using the quantitation ion (m/z 396).

The method was subjected to independent laboratory validation (ILV) using samples of cabbage (head), wheat (grain), orange (fruit) and oilseed rape (seed) fortified with fluopyram at 0.01 ppm and 0.10 ppm. The average recoveries were within acceptable limits (70-120%), and RSDs were <20%.

*Data collection methods:* Samples of crop commodities from the crop field trial, processing, and field rotational crop studies submitted to support this petition were analyzed using three HPLC/MS/MS methods. Samples of crop commodities from the storage stability studies and the European greenhouse studies were analyzed using HPLC/MS/MS methods 00984 or 00984-M001. Samples of crop commodities from the North American crop field trial, processing, and field rotational crop studies were analyzed using HPLC/MS/MS method GM-001-P07-01. The main difference between the methods is the number of analytes that are determined. HPLC/MS/MS method GM-001-P07-01 determines residues of fluopyram *per se*. Method 00984-M001 determines residues of fluopyram and its metabolites AE C656948-benzamide, AE C656948-PCA, and AE C656948-PAA. Method 00984 determines residues of fluopyram, metabolites AE C656948-benzamide, AE C656948-PCA, AE C656948-PAA, as well as rotational crop metabolites AE C656948-7-hydroxy and AE C656948-methyl sulfoxide. The methods are summarized below.

Method 00984: Briefly, residues of fluopyram and metabolites are extracted from crop samples by two successive extractions using a high speed blender with a mixture of ACN:water (80:20, v:v). After a centrifugation step, the extract volume is adjusted. The extracts are then diluted ten times by adding the internal standard of each respective substance: one dilution is performed under acidic conditions, which allows the determination of AE C656948-PCA and AE C656948-methyl-sulfoxide; and in parallel, another dilution is performed under basic conditions, which allows the determination of AE C656948, AE C656948-benzamide, AE C656948-7-hydroxy and AE C656948-PAA sodium (due to the chemical instability of AE C656948-PAA under acidic conditions). The sample extracts are then separated by HPLC and detected by MS/MS, using one injection in positive electrospray ionization for the determination of AE C656948, AE C656948-benzamide, AE C656948-PAA sodium, and AE C656948-7-hydroxy, and another injection in negative electrospray ionization for the determination of AE C656948-PCA and AE C656948-methyl-sulfoxide under different conditions. Quantitation is carried out by internal standardization using the following internal standards: [phenyl-$^{13}C_6$]AE C656948; [phenyl-$^{13}C_6$]AE C656948-benzamide; [2,6-$^{13}C$,$^{15}N$; carboxylic acid-$^{13}C$]AE C656948-PCA; [acetic acid-1,2-$^{13}C_2$/2-$d_2$]AE C656948-PAA sodium; [phenyl-$^{13}C_6$]AE C656948-7-hydroxy; and [methyl-$^{13}CD_3$]AE C653948-methyl-sulfoxide. Two mass transitions are monitored for each analyte. Residues are expressed in parent equivalents.

The LOQ, expressed as parent fluopyram equivalents, is 0.05 ppm for each analyte in wheat straw and 0.01 ppm for each analyte in all other tested sample materials (head lettuce, rape seed, wheat grain, and orange fruit). The calculated LOD ranged from 0.001 to 0.006 ppm (0.002 to 0.011 ppm for wheat straw). Apparent residues in the control samples tested were below 0.3xLOQ (at the MRM transition used for quantitation).

The method was validated in lettuce (head), rape seed, wheat grain, wheat straw, and orange fruit by fortifying samples with each analyte at the LOQ and 10xLOQ. The average recoveries were within acceptable limits (70-120%) and RSDs were <20% for each fortification level, matrix, and analyte using both the quantitation ion and the confirmation ion for all analytes except AE C656948-PCA and AE C656948-methyl-sulfoxide. For AE C656948-PCA in rape seed and AE C656948-methyl-sulfoxide in all tested crops but orange, an interference prevented quantitation at the LOQ at the confirmatory ion transition in all matrices. Recoveries from all matrices at the quantitation ion ranged 68-122% for fluopyram (1 recovery <70% and 1 recovery >120%), 83-116% for AE C656948-benzamide, 61-108% for AE C656948-PCA (1 recovery <70%), 70-102% for AE C656948-PAA, 80-117% for AE C656948-7-hydroxy, and 81-118% for total residues of AE C656948-methyl sulfoxide.

Adequate concurrent method recovery data for fluopyram, AE C656948-benzamide, AE C656948-PCA, and AE C656948-PAA in lettuce, dry pea seed, orange, rape seed, and wheat grain, and for AE C656948-7-hydroxy in lettuce, dry pea seed, rape seed, and wheat grain were submitted for HPLC/MS/MS Method 00984 with the storage stability study, reflecting fortification levels of 0.01 and 0.2 ppm for each analyte in each commodity. In addition, adequate concurrent method recovery data were provided for fluopyram, AE C656948-benzamide, AE C656948-PCA, and AE C656948-PAA in bell pepper, tomato, cucumber, melon, and strawberry with the European greenhouse trials; samples were fortified with each analyte at levels ranging 0.01-2 ppm.

<u>Method 00984-M001</u>: Briefly, residues of fluopyram and metabolites AE C656948-benzamide, AE C656948-PCA, and AE C656948-PAA are extracted from crop samples other than oil using a high speed blender (one extraction) with a mixture of ACN:water (80:20, v:v); residues are extracted from rapeseed oil using liquid/liquid partition with ACN and n-hexane. The ACN/water or ACN extract is filtered, and the volume is adjusted with water (all commodities except rapeseed oil) or water and ACN (rapeseed oil). For the determination of AE C656948, AE C656948-benzamide, AE C656948-PAA, the extracts are diluted under basic conditions and the internal standards are added. For the determination of AE C656948-PCA in/on crop commodities other than rape press cake, an aliquot of the extract is acidified and cleaned up by liquid/liquid partition with methyl-t-butyl-ether (MTBE, dilution 2 times). An aliquot of the MTBE extract is evaporated to dryness and dissolved in the corresponding internal standard solution. For the determination of AE C656948-PCA in/on rape (press cake), an aliquot of the extract is cleaned up on a Varian BondElut-ENV column and an aliquot of the eluate is diluted with the corresponding internal standard solution and ACN:water (30:70, v:v).

The sample extracts are then separated by HPLC and detected by MS/MS, using one injection in positive electrospray ionization for the determination of AE C656948, AE C656948-benzamide, and AE C656948-PAA sodium, and another injection in negative electrospray ionization for the determination of AE C656948-PCA under different conditions. Quantitation is carried out by internal standardization. Two mass transitions are monitored for each analyte. Residues are expressed in parent equivalents.

The LOQ, expressed as parent fluopyram equivalents, is 0.01 ppm for each analyte in all tested sample materials. Apparent residues in control samples using the quantitation MRM transitions were generally below 0.3xLOQ, with the exception of AE C656948-benzamide in grape juice (0.004 ppm) and fluopyram in apple dried pomace (0.003 ppm). It was therefore recommended to use both MRM transitions for analysis and in case of a problem to use the second MRM transition for the quantitation.

The method was validated in apple (fruit, pomace dried, fruit dried, peel rest and sauce), tomato (fruit, juice, puree, and preserve), round cabbage (head and cooking water), grape (bunches of grape, juice, pomace dried, must, and wine), rape (seed, oil, pomace and press cake) and strawberry (fruit, preserve, and jam) by fortifying samples with each analyte at the LOQ and 10xLOQ. The mean recoveries, for each fortification level, for each matrix, and for all analytes, were within 70-120% with the following exceptions: AE C656948-PCA in grape juice: at both 0.01 ppm and 0.1 ppm, a mean recovery of 65% was obtained, with RSD of 11.6% and 0.0% respectively; and AE C656948-PCA in grape must: at 0.01 ppm, a mean recovery of 61% was obtained, with a RSD of 10.9%. Relative standard deviations were below 20% for all analytes and sample materials using the quantitation ion, with the exception of fluopyram in grape pomace dried, at the level 0.01 ppm (RSD = 22.3%).

Recoveries from all matrices ranged from 71-122% for fluopyram (1 recovery >120%), 84-115% for AE C656948-benzamide, 54-107% for AE C656948-PCA (9 recoveries <70%, for grape juice, dried pomace, and must), and 65-118% for AE C656948-PAA (2 recoveries <70%).

Adequate concurrent method recovery data for bell pepper and tomato were submitted for HPLC/MS/MS Method 00984-M001 with the European greenhouse submissions, reflecting fortification levels of 0.01-1.0 ppm for fluopyram, AE C656948-benzamide, AE C656948-PCA, and AE C656948-PAA in each commodity.

<u>Method GM-001-P07-01</u>: Briefly, residues of fluopyram are extracted from homogenized plant matrices using ACN:water (4:1, v:v) by two successive extractions in a high speed blender for at least one minute each. The combined filtrate is mixed with an isotopically labeled internal standard ([phenyl-$^{13}C_6$]AE C656948) and mixed well. In an additional modification to the original method, an aliquot of the sample extract is passed through a small C18 SPE cartridge, and the eluate is diluted with 0.1% aqueous acetic acid for HPLC/MS/MS analysis. Quantitation is carried out by internal standardization; the mass transition monitored is m/z 397.10 to 172.95. The stated LOQ is 0.01 ppm.

No method validation data were provided for this method. Adequate concurrent method recovery data were submitted for this method with each of the North American crop field trial and processing studies, from crop samples fortified at the LOQ and at least one additional fortification level. The fortification levels adequately reflected the observed residues in/on all tested raw agricultural and processed crop commodities.

*Radiovalidation data*: Bayer submitted radiovalidation data for Method 00984-M001 using samples of grape from the grape metabolism studies. More than 97% TRR (total radioactive residues) were extracted from [$^{14}C$]fluopyram-treated grapes using the extraction procedures of Method 00984-M001. The combined residues of AE C656948, AE C656948-benzamide, and AE C656948-pyridyl carboxylic acid accounted for >93% TRR when grape samples were analyzed using the residue analytical method.

No radiovalidation data were provided for Methods 00984 and GM-001-P07-01. The petitioner requested a waiver of radiovalidation data requirements for these methods, with the following justification. The extraction procedure used in the residue analytical methods 00984 and GM-

001-P07-01 comprised two sequential extractions with ACN:water (8:2; v:v). The samples of the metabolism studies were also extracted with ACN:water (8:2; v:v): for the potato, bean, and red pepper metabolism studies, each crop matrix was extracted three times with ACN:water (8:2; v:v); and the samples from the confined rotational crop studies (Swiss chard, turnip roots, turnip leaves, and wheat forage, hay, straw, and grain) were extracted three to four times with ACN:water (8:2; v:v).

The first two extraction steps with ACN:water (8:2; v:v) released:

- >89% TRR in all RACs of the target crop metabolism studies
- >91% TRR in turnip leaves, turnip roots, Swiss chard, and wheat forage of the confined rotational crop (CRC) studies
- >84% TRR in wheat hay and straw of the CRC studies
- ≥70% TRR in wheat grain of the CRC studies

For wheat hay, grain, and straw, additional radioactivity was released with additional extractions (using microwave conditions for hay and straw or diastase enzyme for grain). For hay and straw, the microwave extracts showed the same metabolic profiles as the conventional extracts. For grain, the released radioactivity was characterized as natural compounds (e.g., starch).

No radiovalidation data were submitted for the proposed enforcement method, DFG S 19. However, the petitioner submitted bridging data comparing the extraction procedures of the data collection methods with the extraction procedures of the proposed enforcement method. Samples of tomato from the U.S. field trials were separately extracted using acetone (the extraction solvent of the proposed enforcement method) and ACN:water (4:1, v:v; the extraction solvent of the data collection methods). The extraction of aged fluopyram residues from tomatoes using acetone yielded 101% (average of four samples) of the residues that were extracted using ACN:water (4:1, v:v;), indicating that blending a crop sample in acetone is acceptable for complete extraction of fluopyram residues.

*Conclusions*. The submitted residue analytical method data are adequate to satisfy data requirements for crop commodity methods. Adequate validation data have been provided for the methods used for data collection and the proposed enforcement method. Adequate ILV data have been submitted for the proposed enforcement method. Radiovalidation data are not needed since the solvents used in the enforcement and data gathering methods extract the bulk of the TRR in the plant metabolism studies and aged residues from crop field trials. Because three ions are monitored by GC/MSD in the proposed enforcement method, confirmatory analysis procedures are not needed. The DFG Method S 19 will be forwarded to FDA for publication in PAM Vol. II.

<u>Livestock commodities</u>

First Entry Monograph for Fluopyram, Section B.5.2.2 (MRIDs 47372540-47372542)

Bayer has proposed an HPLC/MS/MS method for the enforcement of tolerances for fluopyram residues in livestock commodities. Method 01079 determines residues of fluopyram and its metabolite AE C656948-benzamide in livestock tissues, milk, and eggs.

<u>Method 01079</u>: Briefly, residues of fluopyram and AE C656948-benzamide are extracted from milk, fat, and egg using a mixture of ACN:water (4:1, v:v). For muscle, kidney, and liver,

samples are extracted twice with ACN:water (4:1, v:v) using microwave heating (120 ºC for 20 minutes). After filtration, the extracts are cleaned up on a C18 cartridge. Internal standards of [phenyl-$^{13}C_6$]fluopyram and [phenyl-$^{13}C_6$]AE C656948-benzamide are added when quantitation is to be performed against internal standard, and the extract is diluted to volume with ACN:water (4:1, v:v). Aliquots of the extracts are further diluted with a mixture of methanol:water (1:9, v:v) containing 10 mM ammonium formate and 120 μL/L formic acid. The sample extracts are then analyzed by HPLC/MS/MS. The residues are determined by external calibration using internal standards or matrix-matched standards. Two mass transitions are monitored for each analyte. Residues are expressed in parent equivalents.

The LOQ is 0.01 ppm and the calculated LOD is 0.003 ppm for each analyte in each matrix. The petitioner stated that residues in control samples were well below 30% of the respective LOQ level.

The method was adequately validated using cattle milk, fat, muscle, liver, and kidney, and hen whole egg fortified with fluopyram and AE C656948-benzamide, each at 0.01 and 0.10 ppm. The average recoveries were within acceptable limits (70-120%), and RSDs were <20% for each analyte in each matrix using both internal standards and matrix-matched standards. Recoveries from all matrices using the quantitation ion (both internal and matrix-matched standards) ranged from 69-105% for fluopyram (1 recovery <70%) and 74-108% for AE C656948-benzamide.

The method was subjected to ILV using samples of milk, eggs, beef muscle, and beef liver fortified with fluopyram and AE C656948-benzamide, each at 0.01 and 0.10 ppm. The average recoveries were within acceptable limits (70-120%), and RSDs were <20% for each analyte in each matrix using both internal standards and matrix-matched standards.

*Data collection method:* Samples of livestock commodities from the cattle and hen feeding studies submitted with this petition were analyzed for residues of fluopyram and its metabolites AE C656948-benzamide, AE C656948-olefine (E-isomer) and AE C656948-olefine (Z-isomer) using HPLC/MS/MS Method 01061. The method is very similar to Method 01079; the main difference is that Method 01061 includes determination of AE C656948-olefines.

Briefly, residues of fluopyram, AE C656948-benzamide, AE C656948-olefine (E-isomer), and AE C656948-olefine (Z-isomer) are extracted from milk, cream, skim milk, hen muscle, hen liver, cattle and hen fat, and egg using ACN:water (4:1, v:v). For cattle muscle, cattle kidney, and cattle liver, samples are extracted twice with ACN:water (4:1, v:v) using microwave heating (120 ºC for 20 minutes). After filtration, the extracts are cleaned up on a Mega Bond Elut-C18 cartridge. Internal standards are added, and the extract is diluted to volume with ACN:water (4:1, v:v). Aliquots of the extracts are further diluted with a mixture of methanol:water (1:9, v:v) containing 10 mM ammonium formate and 120 μL/L formic acid. The sample extracts are then analyzed by HPLC/MS/MS. The residues are determined by external calibration using internal standards. Internal standards of [phenyl-$^{13}C_6$]fluopyram and [phenyl-$^{13}C_6$]AE C656948-benzamide are used; for AE C656948-olefine (E-isomer) and AE C656948-olefine (Z-isomer), the fluopyram internal standard was used for quantitation. Two mass transitions are monitored for each analyte. Residues are expressed in parent equivalents.

The validation of the two individual olefine isomers, AE C656948-olefine (E-isomer) and AE C656948-olefine (Z-isomer) was not possible due to not repeatable internal conversion (E ↔ Z).

Therefore, the calculated residue results are presented as the sum of the two isomers (expressed as parent equivalents).

The LOQ is 0.01 ppm for fluopyram and AE C656948-benzamide in all matrices and 0.02 ppm for the total residues of AE C656948-olefine (E-isomer) and AE C656948-olefine (Z-isomer) in all matrices. The LOD was estimated to be 0.003 ppm for fluopyram, 0.001 ppm for AE C656948-benzamide, and 0.004 ppm for the total residues of AE C656948-olefine (E-isomer) and AE C656948-olefine (Z-isomer) in all matrices.

The method was validated in cattle milk, milk fat, skim milk, liver, muscle, kidney, and fat, and hen whole egg, egg yolk, egg white, muscle, and liver by fortifying each matrix with each analyte at 0.01 ppm and 0.10 ppm. The average recoveries were within acceptable limits (70-120%), and RSDs were <20% for each fortification level, analyte, and matrix. Recoveries from all matrices using the quantitation ion ranged from 85-104% for fluopyram, 86-109% for AE C656948-benzamide, and 68-109% for total residues of AE C656948-olefines (E- and Z-isomers; 1 recovery <70%).

*Extraction efficiency/Radiovalidation:* The petitioner provided data demonstrating the extraction efficiency of the livestock commodity methods using samples from the hen and goat metabolism studies reflecting dosing with [phenyl-UL-$^{14}$C]fluopyram. The extraction procedures of the livestock commodity analytical methods are very similar to those used in the metabolism studies. For matrices other than goat muscle, liver, and kidney, the petitioner provided data showing the %TRR extracted from each matrix in the metabolism studies with a single extraction (the procedures of the analytical method). For goat muscle, liver, and kidney, where the extraction procedures differed from the ones used in the analytical method, radiovalidation experiments were performed within the metabolism study, using the procedures of the analytical method. The extraction efficiencies ranged from 84-97% for all matrices. These data are adequate to satisfy radiovalidation data requirements for the livestock commodity methods.

*Conclusions*. The submitted data are adequate to satisfy data requirements. For the livestock commodity methods, adequate validation data were provided for each analyte. The enforcement method includes adequate confirmatory procedures. Adequate data have been provided to satisfy radiovalidation requirements.

**860.1360 Multiresidue Methods**

First Entry Monograph for Fluopyram, Section B.5.2 (MRID 47372548)

Bayer CropScience submitted data on the testing of fluopyram and its metabolite AE C656948-benzamide using the multiresidue method protocols of FDA PAM Volume I, third edition. Fluopyram and AE C656948-benzamide were tested according to Protocols A, C, D, and F of the FDA PAM Vol. I testing procedures.

Protocol A of the PAM Vol. I testing procedures is not suitable for the detection of either fluopyram or AE C656948-benzamide because neither compound is an N-methyl carbamate and neither compound is naturally fluorescent. Because the compounds are not acids or phenols, they were not tested under Protocol B. Protocol C was tested as per protocol guidelines. Fluopyram and AE C656948-benzamide (DG7 Level II) were deemed suitable for GC analysis and further testing using Protocols D and F was conducted according to the decision tree. Protocol G was not tested because the compounds are not substituted ureas.

Using Protocol D, adequate recovery of fluopyram was obtained using E1 extraction with no Florisil cleanup; recoveries were 90-111% from samples of whole apple fortified at 0.10 and 0.80 ppm. However, fluopyram could not be recovered through the Florisil column cleanup procedures; therefore, Protocols E and F are not appropriate for fluopyram.

AE C656948-benzamide could not be recovered through the Florisil column cleanup procedures of Protocol D or F; therefore, no further testing of this compound was conducted.

The data indicate that the FDA multiresidue methods are suitable for detection and enforcement of fluopyram in non-fatty matrices by Protocol D (Section 302), using E1 extraction and DG17 detection without Florisil cleanup, but are not suitable for detection of AE C656948-benzamide residues.

*Conclusions*. The submitted data are adequate to satisfy data requirements.

**860.1380 Storage Stability**

First Entry Monograph for Fluopyram, Section B.7.6.2 (MRIDs 47372549, 47372550, 48239911, 48239912, and 48239913)

Bayer CropScience submitted three storage stability studies: one study with head lettuce, wheat grain, dry pea seed and rape seed; one study with orange fruit; and one study with dry pea, rape seed and orange fruit.

One study was conducted to investigate the stability of residues of fluopyram and its metabolites AE C656948-benzamide, AE C656948-PCA, AE C656948-PAA, and AE C656948-7-hydroxy under freezer conditions at ~≤-18 °C. Samples of lettuce (head), wheat grain, dry pea seed, and rape seed were spiked with 0.20 ppm each of fluopyram, AE C656948-benzamide, and AE C656948-PAA (as the sodium salt); samples of dry pea seed and rape seed were spiked with 0.20 ppm of AE C656948-PCA; and samples of lettuce and wheat grain were spiked with 0.20 ppm of AE C656948-7-hydroxy. The fortified samples were stored in plastic containers at ~≤-18 °C for nominal storage intervals of 0, 3, 6, 13, 18, 24 and 36 months.

After a deep-freezer storage period of 36 months, the average corrected recovery values (corrected for average concurrent recovery) ranged from 106-110% for fluopyram, 93-99% for AE C656948-benzamide, 97-106% for AE C656948-PCA, 79-102% for AE C656948-PAA and 102-107% for AE C656948-7-hydroxy. These data indicate that fluopyram and its metabolites AE C656948-benzamide and AE C656948-PAA are stable for at least 36 months at ~≤-18 °C in/on lettuce, wheat grain, rape seed, and dry pea seed; that metabolite AE C656948-PCA is stable for at least 36 months at ~≤-18 °C in/on dry pea seed and rape seed; and that metabolite AE C656948-7-hydroxy is stable for at least 36 months at ~≤-18 °C in/on lettuce and wheat grain (see Table 6).

Another study was conducted to investigate the stability of residues of fluopyram and its metabolites AE C656948-benzamide, AE C656948-PCA, and AE C656948-PAA in orange under freezer conditions at ~≤-18 °C. Samples of orange fruit were spiked with 0.20 ppm of each analyte and stored in plastic containers at ~≤-18 °C for nominal storage intervals of 0, 4, 6, 12, 18, 24 and 36 months. Mean recovery values after corrected for mean concurrent recoveries were 100% for AE C656948, 103% for AE C656948-benzamide, 102% for AE C656948-PCA, and 60% for AE C656948-PAA. Other than AE C656948-PAA, recoveries measured for the remaining 3 compounds at the 7 storage intervals in orange were all >90%. For AE C656948-PAA, recoveries declined gradually from103% at 0 month to 69% at 24 months and 60% at 36 months.

Also submitted were stability data for AE 1344122 (AE C656948-methyl-sulfoxide) and BCS-AA 10065 (AE C656948-7-hydroxy) in dry pea seed, rape seed and orange under deep freeze storage for up to 24 or 25 months. Samples of dry pea seed, rape seed and orange fruit were spiked with 0.20 ppm of each analyte and stored at ~≤-18 °C for nominal storage intervals of 0, 4, 6, 12, 18, and 24 months. Mean recovery values after corrected for mean concurrent recoveries ranged from 92-93% for the methylsulfoxide metabolite and from 97-102% for the 7-hydroxy metabolite. These data indicate that AE 1344122 and BCS-AA 10065 are stable for at least 24 months under frozen conditions in dry pea seed, rape seed and orange fruit.

At each storage interval, residues of fluopyram and its metabolites were determined using high performance liquid chromatography/tandem mass spectrometry (HPLC/MS/MS) Method 00984. The mean of the concurrent recoveries were within the acceptable range of 70-110% for all matrices and for all fortification levels. In the control samples, the residues of all compounds were below the LOQ (<0.01 mg/kg for each analyte expressed as AE C656948 parent).

**Table 6. Storage Stability of Fluopyram and its Metabolites in Months**

| | Head lettuce - Water | Wheat grain - Starch | Dry pea - Protein | Rape - Oil | Orange - Acid |
|---|---|---|---|---|---|
| Fluopyram | 36 | 36 | 36 | 36 | 36 |
| Benzamide | 36 | 36 | 36 | 36 | 36 |
| PCA | | | 36 | 36 | 36 |
| PAA | 36 | 36 | 36 | 36 | 24 |
| 7-OH | 36 | 36 | 24 | 24 | 24 |
| Sulfoxide | | | 24 | 24 | 24 |

The storage durations and conditions of samples from the crop field trial, processing and field rotational crop studies submitted to support this petition are presented in Table 7.

**Table 7. Summary of Storage Conditions and Durations of Samples from Crop Field Trial, Processing, and Field Rotational Crop Studies.**

| Matrix | Storage Temperature (°C) | Actual Storage Duration (days) |
|---|---|---|
| **Primary Crop Raw Agricultural Commodities[1]** | | |
| Potato, tuber | <0 | 312-623 |
| Sugar beet, root | <0 | 338-573 |
| Sugar beet, tops | <0 | 498-573 |
| Dried bean, seed | <0 | 331-439 |
| Soybean, seed | <0 | 249-518 |
| Soybean, forage | <0 | 490-581 |
| Soybean, hay | <0 | 498-588 |

**Table 7. Summary of Storage Conditions and Durations of Samples from Crop Field Trial, Processing, and Field Rotational Crop Studies.**

| Matrix | Storage Temperature (°C) | Actual Storage Duration (days) |
|---|---|---|
| Cucurbit vegetable, group 9 | | |
| Cucumber | <0 | 146-280 |
| Cucumber - greenhouse (Europe) | <0 | 176-338 |
| Muskmelon | <0 | 160-219 |
| Muskmelon - greenhouse (Europe) | <0 | 119-313 |
| Summer squash | <0 | 203-282 |
| Apple | <0 | 64-451 |
| Stone fruit, group 11 | | |
| Cherry | <0 | 528-562 |
| Peach | <0 | 179-546 |
| Plum | <0 | 290-543 |
| Grape | <-15 | 49-401 |
| Strawberry | <0 | 78-231 |
| Strawberry - greenhouse (Europe) | ≤-18 | 217-271 |
| Tree nut, group 14 | | |
| Almond | <0 | 591-655 |
| Almond, hull | <0 | 576-640 |
| Pecan | <0 | 501-564 |
| Cereal grain, group 15, except rice | | |
| Corn, field, grain | <0 | 214-390 |
| Sorghum, grain | <0 | 258-374 |
| Wheat, grain | <0 | 23-411 |
| Corn, sweet, K+CWHR | <0 | 373-437 |
| Forage, fodder and straw of cereal grain, group 16, except rice | | |
| Corn, field, stover | <0 | 248-372 |
| Corn, forage | <0 | 238-409 |
| Sorghum, forage | <0 | 263-386 |
| Sorghum, stover | <0 | 285-391 |
| Wheat, forage | <0 | 56-380 |
| Wheat, hay | <0 | 62-453 |
| Wheat, straw | <0 | 50 -411 |
| Banana | <0 | 234-343 |
| Canola, seed | <0 | 151-517 |
| Peanut | <0 | 367-593 |
| Peanut, hay | <0 | 538-583 |
| **Processing/Residue Reduction Studies** | | |
| Apple processed commodities | <-15 | 233-239 |
| Canola processed commodities | <0 | 18-158 |
| Corn processed commodities | <0 | 47-66 |
| Cotton processed commodities | <0 | 8-11 |
| Peanut processed commodities | <0 | 33-112 |
| Plum processed commodities | <-13 | 282-285 |

| Table 7. Summary of Storage Conditions and Durations of Samples from Crop Field Trial, Processing, and Field Rotational Crop Studies. | | |
|---|---|---|
| Matrix | Storage Temperature (°C) | Actual Storage Duration (days) |
| Potato processed commodities | <0 | 308-312 |
| Soybean processed commodities | <-4 | 34-61 |
| Sugar beet processed commodities | <0 | 98-101 |
| Wheat processed commodities | <0 | 4-17 |
| **Field Rotational Crop Studies** | | |
| Alfalfa, forage | <0 | 104-328 |
| Alfalfa, hay | <0 | 104-325 |
| Cotton, undelinted seed [2] | <0 | 140-220 |
| Cotton, gin byproducts | <0 | 179-220 |
| Mustard greens | <0 | 333-405 |
| Turnip, tops | <0 | 329-405 |
| Turnip, roots | <0 | 332-405 |
| Wheat, forage | <0 | 389-405 |
| Wheat, hay | <0 | 331-353 |
| Wheat, straw | <0 | 309-329 |
| Wheat, grain | <0 | 304-325 |

[1] From crop field trial and processing studies.
[2] From field rotational crop and processing study.

*Conclusions*. The submitted data are adequate to satisfy data requirements.

The crop commodities used in the storage stability studies represent commodities containing water (lettuce), starch (wheat grain), protein (dry pea seed), oil (rape seed), and acid (orange). It is concluded that, upon frozen storage, residues of fluopyram and its metabolite AE C656948-benzamide are stable for at least 36 months in water-, starch-, protein-, oil-, and acid-containing materials, and residues of AE C656948-PCA and AE C656948-methyl-sulfoxide are stable for at least 36 and 24 months, respectively, in protein-, oil-, and acid-containing materials. It is also concluded that residues of AE C656948-PAA are stable for at least 36 months in water-, starch-, protein-, and oil-containing materials, and for 24 months in acid-containing materials. Furthermore, residues of AE C656948-7-hydroxy are stable for at least 36 months in water- and starch-containing materials and for at least 24 months in protein-, oil-, and acid-containing materials.

## 860.1400 Water, Fish, and Irrigated Crops

There are no proposed uses that are relevant to this guideline topic.

## 860.1460 Food Handling

There are no proposed uses that are relevant to this guideline topic.

## 860.1480 Meat, Milk, Poultry, and Eggs

First Entry Monograph for Fluopyram, Sections B.7.8.1 and B.7.8.2 (MRIDs 47372601 and 47372602)

There are livestock feedstuffs associated with the 2011 revised proposed uses of fluopyram, and the following ones are considered important: alfalfa hay, alfalfa meal, almond hulls, canola meal, field/sweet corn forage/silage, sorghum grain, sugar beet molasses, and wheat milled byproducts (email, J. Stokes, 5/16/2011). In estimating the livestock dietary burdens, residue values in alfalfa hay and meal are based on the extensive field rotational crop data, and almond hulls and sugar beet molasses are based on the foliar (primary) crop data. Since the proposed label permits limited crop rotation to canola, cereal grains, corn, and soybean with which there are feed items, and since extensive field rotational crop data are not available, the residue values used for canola meal, field/sweet corn forage/silage, sorghum, and wheat milled byproducts are based on half of the primary crop values (see ChemSAC minutes, 6/29/2011 and p. 88): 2.76 ppm for field corn forage/silage (see Appendix III, Figure III-18: maximum residue=5.52 ppm), 1.62 ppm for sorghum grain, 0.30 ppm for wheat milled byproducts, and 0.075 ppm for canola meal (Appendix III, Figure III-2; since this is a blended item, the average value of 0.51 ppm in seed was used to estimate residue level in canola meal, adjusted with a processing factor of 0.3x as indicated in Table 26). As a result, the estimated dietary burdens of fluopyram to livestock, as presented in Table 8, are conservative. The estimated dietary burdens are 1.90 ppm for beef cattle, 3.39 ppm for dairy cattle, 1.24 ppm for poultry, and 1.33 ppm for swine. Bayer submitted feeding studies with cattle and poultry, which are summarized below.

**Table 8. Calculation of Dietary Burdens of Fluopyram Residues to Livestock.**

| Feedstuff | Type[1] | % Dry Matter[2] | % Diet[2] | Maximum Residue (ppm) | Dietary Contribution (ppm)[3] |
|---|---|---|---|---|---|
| **Beef Cattle: 15% R, 80% CC, 5% PC** | | | | | |
| Corn, field, forage/silage | R | 40 | 15 | 2.76 | 1.04 |
| Sorghum, grain, grain | CC | 86 | 40 | 1.62 | 0.75 |
| Wheat, milled byproducts | CC | 88 | 30 | 0.30 | 0.10 |
| Beet, sugar, molasses | CC | 75 | 10 | 0.026 | 0.0035 |
| Canola, meal | PC | 88 | 5 | 0.075 | 0.0043 |
| TOTAL BURDEN | -- | -- | 100 | -- | **1.90** |
| **Dairy Cattle: 45% R, 45% CC, 10% PC** | | | | | |
| Almond, hulls | R | 90 | 5 | 6.12 | 0.34 |
| Corn, sweet, forage/silage | R | 48 | 40 | 2.76 | 2.3 |
| Sorghum, grain, grain | CC | 86 | 35 | 1.62 | 0.66 |
| Beet, sugar, molasses | CC | 75 | 10 | 0.026 | 0.0035 |
| Canola, meal | PC | 88 | 10 | 0.075 | 0.085 |
| TOTAL BURDEN | -- | -- | 100 | -- | **3.39** |

| Table 8. Calculation of Dietary Burdens of Fluopyram Residues to Livestock. | | | | | |
|---|---|---|---|---|---|
| Feedstuff | Type[1] | % Dry Matter[2] | % Diet[2] | Maximum Residue (ppm) | Dietary Contribution (ppm)[3] |
| **Poultry: 75% CC, 25% PC** | | | | | |
| Sorghum, grain, grain | CC | 86 | 75 | 1.62 | 1.22 |
| Canola, meal | PC | 88 | 15 | 0.075 | 0.011 |
| Alfalfa, meal | PC | 89 | 5 | 0.16 | 0.008 |
| Untreated | PC | -- | 5 | -- | -- |
| TOTAL BURDEN | -- | -- | 100 | -- | **1.24** |
| **Swine: 85% CC, 15% PC** | | | | | |
| Sorghum, grain, grain | CC | 86 | 80 | 1.62 | 1.30 |
| Wheat, milled byproducts | CC | 88 | 5 | 0.30 | 0.015 |
| Canola, meal | PC | 88 | 15 | 0.075 | 0.011 |
| TOTAL BURDEN | -- | -- | 100 | -- | **1.33** |

1 R: Roughage; CC: Carbohydrate concentrate; PC: Protein concentrate.
2 OPPTS 860.1000 Table 1 Feedstuffs (June 2008).
3 Contribution = ([residue /% DM] X % diet) for beef and dairy cattle; contribution = ([residue] X % diet) for poultry and swine.

Cattle: Four treatment groups of three dairy cows each were dosed orally for 29 consecutive days with fluopyram at nominal dose levels of 23 mg/capsule, 232 mg/capsule, 696 mg/capsule and 2323 mg/capsule; the actual dosing rates (based on feed consumption) were 1.5 ppm dry feed (dose group B), 14.4 ppm dry feed (dose group C), 44.1 ppm dry feed (dose group D), and 133.1 ppm dry feed (dose group E). Additionally, three dairy cows (dose group F) were fed at 145.9 ppm dry feed for 29 consecutive days, followed by untreated feed for another 7 days (one cow), 14 days (one cow), and 21 days (one cow) in order to investigate the depuration of fluopyram and its metabolites in milk and tissues. One cow was not dosed to serve as a control (dose group A). The dosing levels of the groups identified by the petitioner as B, C, D, E, and F represent 0.79x, 7.6x, 23x, 70x, and 77x, respectively, the dietary burden to beef cattle and 0.44x, 4.2x, 13x, 39x, and 43x, respectively, the dietary burden to dairy cattle.

Cows were milked twice daily. Duplicate milk samples from the animals of the groups A, B, C, D, and E were taken on Day 1, 2, 4, 8, 10, 13, 17, 21, 24, 26 and 29 after the first administered dose. Milk was additionally collected from the animals of dose group F on Day 21, 24, 26, 29, 31, 34, 36, 38, 41, 43, 45, 47, and 50. Cows were sacrificed less than 24 hours after the final dose; cows from the depuration study were sacrificed 7, 14, and 21 days after the last dosing. Samples of liver, muscle, kidney, and fat (perirenal, subcutaneous, and mesenteric) were taken for analysis. Samples of cream (milk fat) and skim milk were generated from milk samples collected on study Day 21 (high dose group only).

Samples of cattle matrices were analyzed for residues of fluopyram and its metabolites AE C656948-benzamide, and AE C656948-olefine (E- and Z-isomers) using HPLC/MS/MS Method 01061. This method was adequate for data collection based on acceptable method recoveries. The validated LOQs in each matrix were 0.01 ppm for fluopyram and AE C656948-benzamide (expressed in parent equivalents) and 0.02 ppm for combined residues of the E and Z isomers of AE C656948-olefine (expressed in parent equivalents).

Milk and tissue samples were stored frozen (≤-18 ºC) prior to analysis, and all analyses were completed within 30 days of collection; therefore, no supporting storage stability data are required.

The results of the cattle feeding study are summarized in Table 9. In milk, residues of fluopyram appeared to reach a plateau by Day 4; residues of AE C656948-benzamide and AE C656948-olefines appeared to reach a plateau by Day 8. Residues of fluopyram and AE C656948-benzamide were highest in liver, and residues of AE C656948-olefines were highest in fat. Residues of each analyte showed a clear dose-response for all tissues.

Milk taken from dose group E (133.1 ppm) was separated by centrifugation into skim milk and milk fat. The fat content of each of the milk fat samples was determined; the average fat content was 73.8%. Residues of fluopyram in skim milk and milk fat were 0.02 ppm and 1.1-1.4 ppm, respectively, and residues of AE C656948-benzamide in skim milk and milk fat were 1.4-1.5 ppm and 0.72-0.98 ppm, respectively; combined residues of fluopyram and AE C656948-benzamide were 1.42-1.52 ppm and 2.08-2.12 ppm in milk fat. The total residues of AE C656948-olefines in skim milk and milk fat were below the LOD and 0.78-1.3 ppm, respectively.

The data indicate that quantifiable residues of AE C656948-benzamide occur in all cattle matrices at all dosing levels; quantifiable residues of fluopyram were observed in liver at all dosing levels, in milk and fat at dosing levels of ≥14.4 ppm, and in muscle and kidney at dosing levels of ≥44.1 ppm.

Transfer factors for fluopyram and AE C656948-benzamide were calculated for each matrix at each feeding level, using the maximum observed residue level for tissues and the average residue level for milk (the average residues were used for milk because milk is a commodity that is typically blended). The calculated transfer factors are presented in Table 10.

| **Table 9.** | **Maximum Residues of Fluopyram, AE C656948-Benzamide[1], and AE C656948-Olefines[1] in Cattle Commodities by Feeding Level.** | | | |
|---|---|---|---|---|
| Cattle Matrix | 1.5 ppm | 14.4 ppm | 44.1 ppm | 133.1 ppm |
| **Fluopyram** | | | | |
| Milk (Day 4 to end)[2] | <0.01 | <0.01-0.02 (average = 0.01) | 0.02-0.09 (average = 0.03) | 0.06-0.17 (average = 0.10) |
| Fat[3] | <0.01 | 0.07 | 0.33 | 0.71 |
| Kidney | <0.01 | <0.01 | 0.05 | 0.08 |
| Liver | 0.26 | 0.98 | 2.8 | 4.0 |
| Muscle | <0.01 | <0.01 | 0.04 | 0.03 |
| **AE C656948-Benzamide** | | | | |
| Milk (Day 8 to end)[2] | 0.01-0.09 (average = 0.02) | 0.15-0.37 (average = 0.22) | 0.40-0.77 (average = 0.54) | 1.1-1.9 (average = 1.5) |
| Fat[3] | 0.01 | 0.33 | 0.45 | 1.1 |
| Kidney | 0.03 | 0.38 | 0.88 | 1.6 |
| Liver | 0.10 | 1.9 | 3.2 | 7.0 |
| Muscle | 0.02 | 0.44 | 0.79 | 1.5 |
| **Combined Residues of Fluopyram and AE C656948-Benzamide** | | | | |
| Milk (Day 8 to end)[2] | <0.02-<0.10 | <0.16-0.39 | 0.42-0.80 | 1.2-2.0 |

| **Table 9. Maximum Residues of Fluopyram, AE C656948-Benzamide[1], and AE C656948-Olefines[1] in Cattle Commodities by Feeding Level.** | | | | |
|---|---|---|---|---|
| Cattle Matrix | 1.5 ppm | 14.4 ppm | 44.1 ppm | 133.1 ppm |
| | (average = 0.03) | (average = 0.23) | (average = 0.57) | (average = 1.6) |
| Fat[3] | <0.02 | 0.37 | 0.78 | 1.6 |
| Kidney | <0.04 | <0.39 | 0.93 | 1.7 |
| Liver | 0.36 | 2.3 | 5.3 | 10.9 |
| Muscle | <0.03 | <0.45 | 0.83 | 1.5 |
| **AE C656948-Olefines** | | | | |
| Milk (Day 8 to end)[2] | <0.02 | ≤0.02 | <0.02-0.05 (average = 0.02) | 0.07-0.14 (average = 0.10) |
| Fat[3] | <0.02 | 0.12 | 0.32 | 0.94 |
| Kidney | <0.02 | <0.02 | 0.04 | 0.15 |
| Liver | <0.02 | 0.06 | 0.13 | 0.58 |
| Muscle | <0.02 | <0.02 | 0.03 | 0.04 |

[1] Residues expressed in parent equivalents.
[2] Range of residues over plateau period.
[3] Includes perirenal, mesenteric, and subcutaneous fat.

| **Table 10. Calculated transfer factors in cattle.[1]** | | | | | |
|---|---|---|---|---|---|
| Commodity | 1.5 ppm | 14.4 ppm | 44.1 ppm | 133.1 ppm | 145.9 ppm |
| **Fluopyram[2]** | | | | | |
| Milk (Day 8 to end) | nd | 0.0007 | 0.0007 | 0.00075 | 0.0069 |
| Fat | nd | 0.005 | 0.0075 | 0.0053 | -- |
| Liver | 0.173 | 0.068 | 0.064 | 0.030 | -- |
| Muscle | nd | nd | 0.0009 | 0.0002 | -- |
| Kidney | nd | nd | 0.001 | 0.0006 | -- |
| **AE C656948-benzamide[2]** | | | | | |
| Milk (Day 8 to end) | 0.01 | 0.015 | 0.012 | 0.011 | 0.017 |
| Fat | 0.007 | 0.023 | 0.010 | 0.008 | -- |
| Liver | 0.067 | 0.13 | 0.073 | 0.053 | -- |
| Muscle | 0.01 | 0.030 | 0.018 | 0.011 | -- |
| Kidney | 0.02 | 0.026 | 0.020 | 0.012 | -- |

[1] Transfer factor calculated by dividing residue value by feeding level. nd = not determined; residues were below the LOQ.
[2] For milk, the transfer factor was calculated using the average residue value over the plateau period (day 8 through study end for the 1.5-, 14.4-, 44.1-, and 133.1-ppm feeding levels, and day 24 through day 29 for the 145.9-ppm feeding level). For all tissues, the transfer factor was calculated using the maximum residue value observed at the specified feeding level.

In the depuration study, the mean residues of fluopyram in milk were 0.11 ppm at the end of the dosing period (Day 29); residues decreased to values below the LOQ for all animals on Day 31 and remained below the LOQ until the end of the study. The mean residues of AE C656948-benzamide in milk were 2.7 ppm at the end of the dosing period (Day 29); mean residues decreased to 0.02 ppm on Day 43 and values below the LOQ were measured from Day 47 until the end of the study. The mean total residues of AE C656948-olefines in milk were 0.13 ppm at the end of the dosing period (Day 29); mean residues decreased to values between 0.03 and 0.04 ppm from Day 36 until sacrifice on Day 43, and then values below the LOQ were measured from Day 47 until the end of the study.

Residues in tissues from the depuration study were determined at sacrifice, on Day 36, 43 and 50. Residues of fluopyram were below the LOD in all samples, with the exception of the liver sample collected on Day 36, where a residue of 0.06 ppm was measured. Residues of AE C656948-benzamide in tissues were quantifiable in all tissues on Day 36 and then decreased on Day 43 and Day 50. In muscle, kidney, and liver, AE C656948-benzamide residues remained at quantifiable levels on Day 50; in fat, residues decreased to levels <LOQ on Day 43 and Day 50.

The total residues of olefines in subcutaneous fat increased from 0.04 ppm on Day 36 to 0.28 ppm on Day 50. Total residues of olefines measured on Day 36 in perirenal and mesenteric fat (0.12 and 0.13 ppm, respectively) increased to 0.21 and 0.26 ppm on Day 43 and reached a total residue level of 0.11 ppm on Day 50. In liver and kidney, the total residues of olefines were quantifiable on Day 36 and decreased on Day 43 and Day 50.

<u>Poultry</u>: Four treatment groups each consisting of 12 laying hens were dosed orally, via feed, for 28 consecutive days with fluopyram at target dose rates of 0, 0.05, 0.50, 1.5, or 5.0 ppm feed. Each treatment group was divided into three subgroups of four hens each. The dosing levels were based on preliminary field residue data and were designated by the petitioner 0.1X (dose group B), 1X (dose group C), 3X (dose group D), and 10X (dose group E) based on the anticipated maximum dietary burden arising from the use of fluopyram in U.S. [the 0.1X group should represent the 1X dose for Europe]. The actual dose levels were 0.05 ppm feed (group B), 0.49 ppm feed (C), 1.6 ppm feed (D) and 4.8 ppm feed (E). Additionally, three groups of laying hens (5 hens/group) were fed at the 10X feeding level (dose group F) for 28 consecutive days in order to investigate the depuration of fluopyram and its metabolites in eggs and tissues thereafter. One control group (9 hens; dose group A) was not dosed. The dosing levels of the groups identified by the petitioner as B, C, D, and E represent 0.04x, 0.40x, 1.2x, and 4.0x, respectively, the dietary burden to poultry.

Eggs were collected from each dose subgroup daily during the dosing period. Eggs were collected for analysis on study days 0, 1, 2, 5, 7, 9, 12, 14, 16, 21, 23, 26, and 28; for the depuration group, eggs were collected for analysis on study days 21, 23, 26, 28, 30, 33, 36, 37, 40, 41, 44, 48, and 49. Hens were sacrificed 3-7 hours after the final dose; for the depuration group, hens were sacrificed on Day 36, Day 41, and Day 49. Samples of liver (entire organ), muscle, and overlaying skin together with any associated fat (and abdominal fat) were collected for analysis.

Samples of hen matrices were analyzed for residues of fluopyram and its metabolites AE C656948-benzamide, and AE C656948-olefine (E- and Z-isomers) using HPLC/MS/MS Method 01061. This method was adequate for data collection based on acceptable method recoveries. The validated LOQs in each matrix were 0.01 ppm for fluopyram and AE C656948-benzamide and 0.02 ppm for combined residues of the E and Z isomers of AE C656948-olefine.

Egg and tissue samples were stored frozen (≤-18 ºC) prior to analysis, and all analyses were completed within 30 days of collection; therefore, no supporting storage stability data are required.

The results of the poultry feeding study are summarized in Table 11. Residues of fluopyram in eggs were below the LOQ of 0.01 ppm in all samples from all dosing groups. Residues of the AE C656948-olefines were below the LOQ of 0.02 ppm in all egg samples from the B, C, and D dose groups; the maximum residues of AE C656948-olefines in eggs from the E dose group were 0.02 ppm. Residues of AE C656948-benzamide in eggs reached a plateau by Day 21 after the first dose. The maximum residues of AE C656948-benzamide in eggs, expressed as parent equivalents, were 0.76 ppm for the E dose group, 0.23 ppm for the D dose group, 0.09 ppm for the C dose group, and below the LOQ of 0.01 ppm for the B dose group.

Residues of fluopyram in tissues were below the LOQ level of 0.01 ppm in all samples. In skin with fat and muscle samples from the B group, AE C656948-benzamide residues were below the LOQ of 0.01 ppm; quantifiable residues of AE C656948-benzamide were found in skin with fat and muscle samples from the higher dose groups. Residues of AE C656948-benzamide were highest in liver, with maximum residues ranging from 0.02 ppm in the B group to 1.6 ppm in the E group. The benzamide residues showed a clear dose-response for tissues.

Residues of AE C656948-olefines in tissues were below the LOQ in all tissues from the B and C dose groups, and were below the LOQ in liver and muscle from the D dose group. Maximum residues of AE C656948-olefines in skin with fat at the D dose group were 0.03 ppm. For the E dose group, maximum residues of AE C656948-olefines were 0.08 ppm for skin with fat, 0.02 ppm for liver, and 0.06 ppm for muscle.

The data indicate that quantifiable residues of AE C656948-benzamide occur in liver at all dosing levels and in egg, skin with fat, and muscle at dosing levels ≥0.49 ppm; no quantifiable residues of fluopyram were observed in poultry matrices at any dosing level.

Transfer factors for fluopyram and AE C656948-benzamide were calculated for each matrix at each feeding level, using the maximum observed residue level for eggs and tissue. The calculated transfer factors are presented in Table 12.

**Table 11. Maximum Residues of Fluopyram, AE C656948-Benzamide[1], and AE C656948-Olefines[1] in Hen Commodities by Feeding Level.**

| Hen Matrix | 0.05 ppm | 0.49 ppm | 1.6 ppm | 4.8 ppm |
|---|---|---|---|---|
| **Fluopyram** | | | | |
| Egg (Day 21 to end)[2] | <0.01 | <0.01 | <0.01 | <0.01 |
| Skin with fat | <0.01 | <0.01 | <0.01 | <0.01 |
| Liver | <0.01 | <0.01 | <0.01 | <0.01 |
| Muscle | <0.01 | <0.01 | <0.01 | <0.01 |
| **AE C656948-Benzamide** | | | | |
| Egg (Day 21 to end)[2] | <0.01 | 0.07-0.09 (average = 0.08) | 0.20-0.23 (average = 0.21) | 0.64-0.76 (average = 0.71) |
| Skin with fat | <0.01 | 0.04 | 0.11 | 0.63 |
| Liver | 0.02 | 0.16 | 0.43 | 1.6 |
| Muscle | <0.01 | 0.04 | 0.10 | 0.33 |
| **Combined Residues of Fluopyram and AE C656948-Benzamide** | | | | |
| Egg (Day 21 to end)[2] | <0.02 | <0.08-<0.10 (average = 0.09) | <0.21-<0.24 (average = 0.22) | <0.65-<0.77 (average = 0.72) |
| Skin with fat | <0.02 | <0.05 | <0.12 | <0.64 |
| Liver | <0.03 | <0.17 | <0.44 | <1.6 |
| Muscle | <0.02 | <0.05 | <0.11 | <0.34 |

| **Table 11.** | **Maximum Residues of Fluopyram, AE C656948-Benzamide[1], and AE C656948-Olefines[1] in Hen Commodities by Feeding Level.** | | | |
|---|---|---|---|---|
| Hen Matrix | 0.05 ppm | 0.49 ppm | 1.6 ppm | 4.8 ppm |
| **AE C656948-Olefines** | | | | |
| Egg (Day 21 to end)[2] | <0.02 | <0.02 | <0.02 | <0.02-0.02 |
| Skin with fat | <0.02 | <0.02 | 0.03 | 0.08 |
| Liver | <0.02 | <0.02 | <0.02 | 0.02 |
| Muscle | <0.02 | <0.02 | <0.02 | 0.06 |

[1] Residues expressed in parent equivalents.
[2] Range of residues over plateau period.

| **Table 12.** | **Calculated transfer factors in poultry.[1]** | | | |
|---|---|---|---|---|
| Commodity | 0.05 ppm | 0.49 ppm | 1.6 ppm | 4.8 ppm |
| **AE C656948** | | | | |
| Egg (Day 21 to end) | nd | nd | nd | nd |
| Skin with Fat | nd | nd | nd | nd |
| Liver | nd | nd | nd | nd |
| Muscle | nd | nd | nd | nd |
| **AE C656948-benzamide** | | | | |
| Egg (Day 21 to end) | nd | 0.18 | 0.14 | 0.16 |
| Skin with Fat | nd | 0.08 | 0.07 | 0.13 |
| Liver | 0.40 | 0.33 | 0.27 | 0.33 |
| Muscle | nd | 0.08 | 0.06 | 0.07 |

[1] Transfer factor calculated by dividing residue value by feeding level. nd = not determined; residues were below the LOQ.

In samples from the depuration study, residues of AE C656948-benzamide and AE C656948-olefine decreased steadily with time in eggs and tissues after the treated feed (F) was withdrawn from the hens. In eggs, average residue of benzamide amounted to 0.83 ppm on Day 28 and decreased steadily to 0.03 ppm on Day 49. The total olefines residues amounted to 0.03 ppm on Day 28 and decreased steadily to < LOQ on Day 49. In skin with fat, liver, and muscle samples from the F dose group, benzamide residues were 0.41 ppm, 1.4 ppm, and 0.29 ppm on Day 28, respectively, and decreased to 0.05 ppm in liver, 0.02 ppm (skin with fat) and 0.01 ppm (muscle) on Day 49. No residues of fluopyram were found in any samples from the depuration study.

*Conclusions*. The submitted studies are adequate to satisfy data requirements. The data indicate that tolerances for fluopyram residues of concern are needed for egg, milk, and the meat, fat, and meat byproducts of cattle, goat, hog, horse, poultry, and sheep.

The maximum anticipated residues of fluopyram and AE C656948-benzamide were calculated using the estimated dietary burdens for fluopyram and the transfer factors reported in Table 10 (cattle and swine commodities) and Table 12 (poultry commodities). The maximum anticipated residues are presented in Table 13.

**Table 13. Maximum Anticipated Residues of Fluopyram and AE C656948-Benzamide in Livestock Commodities Following Dosing at 1x the Dietary Burden.**

| Livestock | Estimated Dietary Burden (ppm) | Matrix | Fluopyram (ppm) | AE C656948-Benzamide (ppm) [1] | Combined residues of Fluopyram and AE C656948-Benzamide (ppm) |
|---|---|---|---|---|---|
| Cattle | 3.39 [2] | Fat | 0.025 | 0.078 | 0.10 |
| | | Muscle | 0.031 | 0.10 | 0.13 |
| | | Kidney | 0.0034 | 0.088 | 0.091 |
| | | Liver | 0.586 | 0.44 | 1.03 |
| | | Milk | 0.0025 | 0.051 | 0.054 |
| Poultry | 1.24 | Fat | <0.01 | 0.161 | 0.17 |
| | | Muscle | <0.01 | 0.100 | 0.11 |
| | | Liver | <0.01 | 0.500 | 0.51 |
| | | Egg | <0.01 | 0.223 | 0.23 |
| Swine | 1.33 | Fat | 0.010 | 0.031 | 0.041 |
| | | Muscle | 0.0012 | 0.040 | 0.041 |
| | | Kidney | 0.0013 | 0.035 | 0.036 |
| | | Liver | 0.23 | 0.173 | 0.40 |

[1] Expressed as parent equivalents.
[2] Maximum estimated dietary burden for dairy cattle, used to calculate maximum anticipated ruminant residues.

Based on the maximum anticipated residues, HED concludes that the following tolerances are appropriate for the combined residues of fluopyram and AE C656948-benzamide in livestock commodities: 0.11 ppm for the fat, 0.10 ppm for kidney, and 0.15 ppm for meat of cattle, goat, horse, and sheep; 1.1 ppm for the meat byproducts of cattle, goat, horse, and sheep; 0.06 ppm for milk; 0.04 ppm for kidney of hog; 0.05 ppm for the fat and meat of hog; 0.45 ppm for the meat byproducts of hog; 0.20 ppm for the fat of poultry; 0.15 ppm for the meat of poultry; 0.60 ppm for the meat byproducts of poultry; and 0.25 ppm for egg.

## 860.1500 Crop Field Trials

First Entry Monograph for Fluopyram, Sections B.7.6.1.1 through B.7.6.1.3 (MRIDs 47372603-47372605, 47372608, 47372610, and 47372615)
Second Entry Monograph for Fluopyram, Sections B.7.6.1.4 through 7.6.1.55 (MRIDs 47372603, 47372606, 47567010-47567037, and 47567101)

Bayer submitted crop field trial data from field trials conducted in North America with a variety of crops, as well as data from field trials conducted in Latin America for banana. The relevant studies are described below, and the results are summarized in Table 14 through Table 25. The petitioner additionally submitted data from field trials conducted in Europe with a variety of crops, which included data from studies conducted in greenhouses. For cucumber, melon, and strawberry, the European greenhouse data are discussed below because the data will be used to support greenhouse uses in North America. No other European field trial data are discussed herein.

For the North American field trials, the petitioner collected residue data for fluopyram only.

The Agency's *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* was utilized for determining appropriate tolerance levels based on the submitted crop field trial data for raw agricultural crop commodities. All tolerance calculations are presented in Appendix II and III.

HED notes that for the European greenhouse trials, samples were collected at three or four intervals in addition to the proposed PHI. In each trial, if residues of fluopyram at intervals greater than the proposed PHI exceeded the residue level at the PHI, the higher values were used in data summaries to cover the worst case residue; the higher values were also used for tolerance calculations. HAFT stands for highest averge field trial value.

Also, with the exception of the banana field trials and one grape field trial, no spray adjuvants were used in any of the crop field trials. However, HED has recently reviewed bridging field trials conducted on strawberry, grape, cucumber, bulb onion, potato, lettuce, tomato, peach, apple and almond with and without addition of 0.125% v/v of a non-ionic surfactant (Induce®) and concluded that the addition of the NIS had no significant effect on the residue level concentration on these crops (D384287, S. Funk, 6/8/2011). Therefore, the product label must be amended to specify that non-ionic surfactants at 0.125% v/v may be added to spray mixtures.

Apple

Bayer has submitted magnitude of the residue studies for apple and pear, the representative crops of pome fruit, group 11. The results from the apple field trials are discussed below and summarized in Table 14.

**Table 14. Summary of Residue Data from Apple Field Trials with Fluopyram.**

| Crop matrix | Total Applic. Rate (lb ai/A) [kg ai/ha] | PHI (days) | Fluopyram Residue Levels (ppm) | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | n | Min. | Max. | HAFT | Median | Mean | Std. Dev. |
| **POME FRUIT (proposed use = 0.445 lb ai/A total application rate, 0-day PHI; 7-day revised PHI)** | | | | | | | | | |
| **Two Applications; Concentrate Spray** | | | | | | | | | |
| Apple | 0.440 – 0.461 (0.493 – 0.517) | 7 | 34 | 0.040 | 0.247 | 0.242 | 0.109 | 0.120 | 0.063 |
| **Two Applications; Dilute Spray** | | | | | | | | | |
| Apple | 0.440 – 0.461 (0.493 – 0.517) | 7 | 24 | 0.057 | 0.262 | 0.255 | 0.086 | 0.105 | 0.055 |
| **Four Applications; Concentrate Spray** | | | | | | | | | |
| Apple | 0.477 – 0.479 (0.535 – 0.536) | 7 | 4 | 0.061 | 0.107 | 0.101 | 0.083 | 0.084 | 0.021 |

Seventeen apple trials were conducted in North America in 2006 and 2007. Seventeen apple trials, representing twelve harvest trials and five decline trials, were conducted in Zones 1 (NY, PA, and VA, 3 trials), 2 (GA, 1 trial), 5 (IL, MI, ON, and WI, 7 trials), 9 (UT, 1 trial), 10 (CA, 1 trial), and 11 (ID, OR, and WA, 4 trials).

Two foliar spray applications of the 4.16 lb/gal SC formulation at a rate of 0.214-0.231 lb ai/A (240-259 g ai/ha) were made to apples with a 5- to 7-day application interval, for total application rates of 0.440-0.461 lb ai/A (493-517 g ai/ha). The foliar spray application rates represent ~1x the proposed maximum seasonal rate. For all trials, foliar spray applications were made in concentrate spray volumes, at 39-72 GPA (368-671 L/ha). For 12 of the trials, there was an additional plot in which applications were made with dilute spray volumes, at 208-306 GPA (1941-2860 L/ha). For two of the apple trials, there was an additional plot in which a total of four foliar spray applications, at rates ranging from 0.115 to 0.124 lb ai/A/application (129 to 139 g ai/ha/application) for a total rate ranging from 0.477 to 0.479 lb ai/A (535 to 536 g ai/ha). For these trials, all plots were treated with a low volume spray solution, ranging 51-61 GPA (480-570 L/ha). Duplicate treated samples of apple were harvested on the day of last application (0-day PHI) and 7 days following the last application in the harvest trials and 0, 3, 7, 10, and 14 days following the last application in the decline trials.

The apple samples were analyzed for residues of fluopyram using an adequate HPLC/MS/MS method, Method No. GM-001-P07-01. The LOQ was 0.01 ppm each in/on apple fruit. Sample storage conditions and durations are reported in Table 6; samples were stored frozen for up to ~16 months prior to analysis. The available storage stability data support the apple field trial study.

The results of the apple field trials are summarized in Table 14 (7-day data only). Residues of fluopyram in/on apple fruit at a 7-day PHI for the plots with two applications and concentrate spray volumes ranged from 0.040-0.25 ppm. The mean and HAFT were 0.12 ppm and 0.24 ppm, respectively.

Residues of fluopyram in/on apple fruit at a 7-day PHI for the plots with two applications and dilute spray volumes ranged from 0.057-0.26 ppm. The mean and HAFT were 0.11 ppm and 0.26 ppm, respectively.

Residues of fluopyram in/on apple fruit at a 7-day PHI for the plots with four applications ranged from 0.061-0.11 ppm. The mean and HAFT were 0.084 ppm and 0.10 ppm, respectively.

For all the decline trials, fluopyram residues decreased from the 0-day PHI to the 14-day PHI.

*Conclusions*. The submitted residue data for apple are adequate to fulfill data requirements. The number and locations of the field trials are in accordance with OPPTS Guideline 860.1500 for apple. Field trials were conducted at ~1x the proposed maximum seasonal rate and samples were harvested at the revised PHI.

Based on the available data and the NAFTA tolerance calculator (see Appendix II), a tolerance of 0.30 ppm for residues of fluopyram in/on apple is appropriate.

<u>Dried beans</u>

Bayer has submitted magnitude of the residue studies for dried bean and dried pea seed, representative crops of dried shelled pea and bean, subgroup 6C. The results from the dry bean field trials are discussed below and summarized in Table 15.

**Table 15. Summary of Residue Data from Dry Bean Field Trials with Fluopyram.**

| Crop matrix | Total Applic. Rate (lb ai/A) [kg ai/ha] | PHI (days) | Fluopyram Residue Levels (ppm) | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | n | Min. | Max. | HAFT | Median | Mean | Std. Dev. |

| **Table 15. Summary of Residue Data from Dry Bean Field Trials with Fluopyram.** | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Crop matrix | Total Applic. Rate (lb ai/A) [kg ai/ha] | PHI (days) | Fluopyram Residue Levels (ppm) | | | | | | |
| | | | n | Min. | Max. | HAFT | Median | Mean | Std. Dev. |
| **DRIED BEANS (proposed use = 0.445 lb ai/A total application rate, 0-day PHI; revised use = 0.268 lb ai/A total application rate, 14-day PHI)** | | | | | | | | | |
| Dried bean seed | 0.441-0.452 (0.494-0.507) | 0[1], 13-14 | 18 | <0.01 | 0.076 | 0.068 | 0.012 | 0.024 | 0.021 |

[1] At one trial (n=2), the bean plants were cut from the ground at a 0-day PHI and the seed was sampled 14 days later, after drying in the field. Sample residues from this trial were not the maximum residue or HAFT for the study.

Nine trials, representing eight harvest trials and one decline trial, were conducted in Zones 5 (IA, IL, MN, and NE, 4 trials), 7 (ND, 1 trial), 8 (TX, 1 trial), 9 (ID, 1 trial), 10 (CA, 1 trial), and 11 (ID, 1 trial) on dried beans during the 2006-2007 growing seasons.

Two foliar spray applications of the 4.16 lb/gal SC formulation at a rate of 0.218-0.229 lb ai/A/application (244-257 g ai/ha) were made to dried beans with 5- to 7-day RTIs, for total application rates of 0.441-0.452 lb ai/A (494-507 g ai/ha). The application rates represent ~1.7x the proposed maximum seasonal rate. Applications were made in spray volumes of 10-20 GPA (91-183 L/ha). For all trials except one, duplicate treated samples of dried bean were harvested 13-14 days after the final application in the harvest trials and 0, 7, 14, 17, and 21 days following last application in the decline trial. At one harvest trial, the bean plants were cut from the ground at a 0-day PHI and seed was sampled 14 days later, after drying in the field. There are no feed items involved with the proposed dried beans.

The dried bean seed samples were analyzed for residues of fluopyram using an adequate HPLC/MS/MS method, Method No. GM-001-P07-01. The LOQ was 0.01 ppm in dried bean seed. Sample storage conditions and durations are reported in Table 7; samples were stored frozen for up to ~14 months prior to analysis. The available storage stability data support the dried bean seed field trial study.

The results of the dried bean field trials are summarized in Table 15. Residues of fluopyram in/on dried bean seed at a 13- to 14-day PHI ranged from <0.01-0.076 ppm. The mean and HAFT were 0.024 ppm and 0.068 ppm, respectively. In the decline trial, average residues in/on dried bean seeds declined from the 0-day PHI to the 22-day PHI.

*Conclusions*. The submitted residue data for dried bean are adequate to fulfill data requirements. The number and locations of the field trials are in accordance with OPPTS Guideline 860.1500 for dried bean. Field trials were conducted at ~1.7x the revised maximum seasonal rate for dried seed.

The residue data have been adjusted for rate differential and based on the NAFTA tolerance calculator (see Appendix II), a tolerance of 0.09 ppm for residues of fluopyram in/on dried bean is appropriate.

<u>Grape</u>

Bayer has submitted magnitude of the residue studies for grape. The results from these field trials are discussed below and summarized in Table 16.

| Table 16. Summary of Residue Data from Grape Field Trials with Fluopyram. | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Crop matrix | Total Applic. Rate (lb ai/A) [kg ai/ha] | PHI (days) | Fluopyram Residue Levels (ppm) | | | | | | |
| | | | n | Min. | Max. | HAFT | Median | Mean | Std. Dev. |
| **GRAPE (proposed use = 0.445 lb ai/A total application rate, 7-day PHI; revised to wine grapes only )** | | | | | | | | | |
| Grape | 0.439-0.458 [0.492-0.513] | 6-7 | 32 | 0.096 | 0.950 | 0.948 | 0.372 | 0.401 | 0.229 |

Sixteen trials, representing fifteen harvest trials and one decline trial, were conducted in Zones 1 (NY and PA, 2 trials), 5 (IL, 1 trial; MI, 1 trial; and ON, 2 trials), 10 (CA, 8 trials), and 11 (OR and WA, 2 trials) during the 2006 and 2007 growing seasons.

Two foliar spray applications of the 4.16 lb/gal SC formulation at a rate of 0.217-0.230 lb ai/A/application (243-258 g ai/ha) were made to grapes with 12- to 14-day RTIs, for total application rates of 0.439-0.458 lb ai/A (492-513 g ai/ha). The application rates represent ~1x the proposed maximum seasonal rate. Applications were made in spray volumes of 47-67 GPA (438-627 L/ha). Duplicate treated samples were harvested 3 and 7 days following last application in the harvest trials, and 0, 3, 7, 10, and 14 days following last application in the decline trial.

The grape samples were analyzed for residues of fluopyram using an adequate HPLC/MS/MS method, Method No. GM-001-P07-01. The LOQ was 0.01 ppm in grapes. Sample storage conditions and durations are reported in Table 6; samples were stored frozen for up to ~13 months prior to analysis. The available storage stability data support the grape field trial study.

The results of the grape field trials are summarized in Table 16. Residues of fluopyram ranged from 0.096-0.950 ppm in/on grapes harvested at a 7-day PHI. The mean and HAFT values were 0.401 ppm and 0.948 ppm for the 7-day PHI, respectively. In the decline trial, the mean residue level decreased from the 0-day PHI to the 14-day PHI.

*Conclusions*. The submitted crop field trial data for grape are adequate to satisfy data requirements. The number and locations of the field trials are in accordance with OPPTS Guideline 860.1500 for grape. Field trials were conducted at ~1x the proposed maximum seasonal rate and samples were harvested at the proposed PHI.

Based on the available data and the NAFTA tolerance calculator (see Appendix II), a tolerance of 1.4 ppm for residues of fluopyram in/on grape, wine is appropriate.

<u>Peanut</u>

Bayer has submitted magnitude of the residue studies for peanut. The results from these field trials are discussed below and summarized in Table 17.

| **Table 17. Summary of Residue Data from Peanut Field Trials with Fluopyram.** | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Crop matrix | Total Applic. Rate (lb ai/A) [kg ai/ha] | PHI (days) | Fluopyram Residue Levels (ppm) | | | | | | | |
| | | | n | Min. | Max. | HAFT | Median | Mean | Std. Dev. |
| **PEANUT (proposed use = 0.445 lb ai/A total application rate, 7-day PHI)** | | | | | | | | | |
| Peanut | 0.438 to 0.455 (0.491 to 0.510) | 6-7 | 24 | <0.01 | 0.018 | 0.017 | <0.01 | 0.011 | <0.01 |
| Peanut, hay | 0.438 to 0.455 (0.491 to 0.510) | 6-7 | 24 | 1.08 | 21.88 | 20.66 | 6.19 | 8.72 | 6.78 |

Twelve trials, representing eleven harvest trials and one decline trial, were conducted in Zones 2 (FL, GA, NC, and VA, 7 trials), 3 (FL, 2 trials), 6 (TX, 2 trials), and 8 (TX, 1 trial) during the 2007-2008 growing seasons. One FL trial, conducted in Zone 3, was used to fulfill the requirements for Zone 2 since the trial site was close to the border of Zones 2 and 3.

Two foliar spray applications of the 4.16 lb/gal SC formulation at a rate of 0.216-0.229 lb ai/A/application (242-256 g ai/ha) were made to peanuts with 12- to 14-day RTIs, for total application rates of 0.438-0.455 lb ai/A (491-510 g ai/ha). The application rates represent ~1x the proposed maximum seasonal rate. Applications were made in spray volumes of 10-20 GPA (92-184 L/ha). Duplicate treated samples of peanut nutmeat and hay were harvested 6-7 days after the last application in the harvest trials, and 0, 2, 6, 9, and 13 days following last application in the decline trial. Both commodities were allowed to dry in the field or under shelter for 2 to 17 days, until commercial dryness was obtained.

The peanut RAC samples were analyzed for residues of fluopyram using an adequate HPLC/MS/MS method, Method No. GM-001-P07-01. The LOQ was 0.01 ppm in/on peanut nutmeat and 1.0 ppm in peanut hay. Sample storage conditions and durations are reported in Table 7; samples were stored frozen for up to ~19 months prior to analysis. The available storage stability data support the peanut field trial study.

The results of the peanut field trials are summarized in Table 17. Residues of fluopyram in/on peanut at a 6- to 7-day PHI ranged from <0.01-0.018 ppm. The mean and HAFT were 0.011 ppm and 0.017 ppm, respectively. Residues of fluopyram in/on peanut hay at a 6- to 7-day PHI ranged 1.08-21.88 ppm. The mean and HAFT were 8.72 ppm and 20.7 ppm, respectively. Since residues were low in the nutmeat, residue decline could not be assessed; however, the residues declined from the 0- to the 13-day PHI in the peanut hay decline trial samples.

*Conclusions*. The submitted peanut crop field trial data are adequate to fulfill data requirements. The number and locations of the field trials are in accordance with OPPTS Guideline 860.1500 for use on peanut. Field trials were conducted at ~1x the proposed maximum seasonal rate and samples were harvested at the proposed PHI.

Based on the available data and the NAFTA tolerance calculator (see Appendix II), a tolerance of 0.02 ppm for residues of fluopyram in/on peanut is appropriate. Since the proposed includes a feeding restriction on peanut hay, a tolerance in/on peanut hay is not needed and the proposed peanut hay tolerance should be removed.

Pistachio – see Tree nut, group 14

The proposed use on pistachio is identical to the proposed use on the tree nut crop group. HED has concluded that pistachios are to be a member of the tree nuts crop group [see memo entitled "Reviewer's Guide and Summary of HED ChemSAC Approvals for Amending Crop Group/Subgroups [40 CFR 180.411 and Commodity Definitions [40 CFR 180.1 (h)]" from B. Schneider to B. Madden dated 6/14/06], with almonds and pecans remaining as the representative commodities. Until 40 CFR §180.41 is updated, tolerances for pistachios will be listed separately from the crop group tolerance, but the tolerance will be established at the same level as the crop group. Thus, the available data support a tolerance of 0.05 ppm for fluopyram residues in/on pistachio.

Potato

Bayer has submitted magnitude of the residue studies for potato. The results from these field trials are discussed below and summarized in Table 18.

**Table 18. Summary of Residue Data from Potato Field Trials with Fluopyram.**

| Crop matrix | Total Applic. Rate (lb ai/A) [kg ai/ha] | PHI (days) | Fluopyram Residue Levels (ppm) | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | n | Min. | Max. | HAFT | Median | Mean | Std. Dev. |
| **POTATO (proposed use = 0.445 lb ai/A total application rate, 7-day PHI; revised to 0.356 lb ai/A for ground applications and 0.275 lb ai/A for aerial applications)** | | | | | | | | | |
| Potato, tuber | 0.437 - 0.454 (0.489 - 0.509) | 6-7 | 32 | <0.01 | 0.017 | 0.017 | 0.01 | 0.01 | 0.002 |

Sixteen trials, representing fourteen harvest trials and two decline trials, were conducted in Zones 1 (NY and PA, 2 trials), 2 (VA, 1 trial), 3 (FL, 1 trial), 5 (IL, KS, MN, and NE, 4 trials), 10 (CA, 1 trial), and 11 (ID, OR, and WA, 7 trials) during the 2006 growing season. One ID trial in Zone 11 was used to fulfill the requirements for Zone 9 since the trial was conducted at a site close to the border between Zones 9 and 11.

Two foliar spray applications of the 4.16 lb/gal SC formulation at a rate of 0.211-0.234 lb ai/A/application (236-263 g ai/ha) were made to potato with 3- to 5-day RTIs, for total application rates of 0.437-0.454 lb ai/A (489-509 g ai/ha). The application rates represent ~1.3-1.6x the proposed maximum seasonal rate. Applications were made in spray volumes of 10-19 GPA (93-175 L/ha). Duplicate treated samples were harvested 6-7 days following the last application in the harvest trials, and 0, 3, 7, 14, and 21 days following last application in the decline trials.

The potato samples were analyzed for residues of fluopyram using an adequate HPLC/MS/MS method, Method No. GM-001-P07-01. The LOQ was 0.01 ppm in potato tuber. Sample storage conditions and durations are reported in Table 7; samples were stored frozen for up to ~20 months prior to analysis. The available storage stability data support the potato field trial study.

The results of the potato field trials are summarized in Table 18. Residues of fluopyram in/on potato tubers at a 6- to 7-day PHI ranged from <0.01-0.02 ppm. The mean and HAFT were 0.01 ppm and 0.017 ppm, respectively. In the decline trials, the residue levels were at or below the LOQ at all sampling intervals.

*Conclusions*. The submitted potato crop field trial data are adequate to fulfill data requirements. The number and locations of the field trials are in accordance with OPPTS Guideline 860.1500 for tuberous and corm vegetables subgroup 1C. Field trials were conducted at ~1.3-1.6x the proposed maximum seasonal rate and samples were harvested at the proposed PHI.

Since >60% of the samples resulted in residues <0.01 ppm the NAFTA tolerance calculator was not used. Based on the maximum field trial residue, HED concludes that a tolerance of 0.02 ppm for residues of fluopyram in/on potato is appropriate.

Strawberry

Bayer has submitted magnitude of the residue studies for strawberry. The results from these field trials are discussed below and summarized in Table 19.

**Table 19. Summary of Residue Data from Strawberry Field Trials with Fluopyram.**

| Crop matrix | Total Applic. Rate (lb ai/A) [kg ai/ha] | PHI (days) | Fluopyram Residue Levels (ppm) | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | n | Min. | Max. | HAFT | Median | Mean | Std. Dev. |
| **STRAWBERRY (proposed use = 0.445 lb ai/A total application rate, 0-day PHI for spray uses and drip application and 1-day PHI greenhouse uses; revised to delete field spray use)** | | | | | | | | | |
| Strawberry - drip irrigation field | 0.442-0.468 [0.495-0.525] | 0 | 20 | <0.01 | 0.112 | 0.10 | 0.010 | 0.026 | 0.028 |
| Strawberry - greenhouse spray (European data) | 0.446 [0.500] | 1 | 8 | 0.12 | 0.79 | 0.79 | 0.27 | 0.35 | 0.26 |

Ten trials, representing nine harvest trials and one decline trial, were conducted in Zones 1 (PA, 1 trial), 2 (GA, 1 trial), 3 (FL, 1 trial), 5 (IA, MI, and MN, 3 trials), 10 (CA, 3 trials), and 12 (OR, 1 trial) during the 2007 growing season.

Each trial consisted of two treatment plots, a spray treated plot and a drip irrigation plot. For the spray treated plot, two foliar spray applications of the 4.16 lb/gal SC formulation at a rate of 0.217-0.235 lb ai/A/application (243-263 g ai/ha) were made to strawberry plants with 5- to 6-day RTIs, for total application rates of 0.438-0.463 lb ai/A (491-525 g ai/ha). A second treated plot received two drip irrigation applications of the 4.16 lb/gal SC formulation at a rate of 0.221-0.234 lb ai/A/application (248-262 g ai/ha) with 5- to 6-day RTIs, for total application rates of 0.442-0.468 lb ai/A (495-525 g ai/ha). The application rates represent ~1x the proposed maximum seasonal rate. Spray applications were made in spray volumes of 5-20 GPA (47-189 L/ha). For drip irrigation, there was a minimum of one emitter per plant with all plants having an equal number of emitters; application volumes were 0.27-0.57 gal/hr/emitter (1.0-2.2 L/hr/emitter). Duplicate treated samples were harvested on the day of last application for both treatment plots; samples were additionally harvested 7 days after last application from the drip irrigation plots. At one site, duplicate samples were collected at intervals of 0, 3, 7, 10, and 14 days following the last application in both plots to evaluate residue decline.

The strawberry samples were analyzed for residues of fluopyram using an adequate HPLC/MS/MS method, Method No. GM-001-P07-01. The LOQ was 0.01 ppm in strawberries. Sample storage conditions and durations are reported in Table 7; samples were stored frozen for up to ~8 months prior to analysis. The available storage stability data support the strawberry field trial study.

The results of the strawberry field trials are summarized in Table 19. For the drip irrigation trials, fluopyram in/on strawberry at the 0-day PHI ranged from <0.01 to 0.11 ppm. The mean and HAFT values were 0.026 ppm and 0.10 ppm for the 0-day PHI, respectively. In the decline trial, the residue level at the 0-day PHI was <0.01 ppm, and residues increased to about 0.03 ppm at 10 and 14 days after last treatment. The residue levels in the drip irrigation trials were 5 to 10 times lower than those observed in the broadcast application trials.

<u>Europe</u>: Eight greenhouse trials on strawberry were conducted during the 2006 and 2007 growing seasons according to the critical European GAP. The greenhouse trials were located in Spain, Italy, Germany (2), Netherlands, northern France, United Kingdom, and Belgium.

In the greenhouse trials, the 4.16 lb/gal SC formulation was applied as sprays twice with an application rate of 0.5 L/ha and 300-1000 L water per ha, corresponding to a spray concentration of 0.05-0.17% and a rate of 0.25 kg ai/ha/application. The applications were carried out with 6- to 7-day RTIs with the last application approximately 1 day prior to the expected date of harvest. Total application rates were 0.50-0.54 kg ai/ha (0.446-0.482 lb ai/A), corresponding to 1x the proposed maximum seasonal rate. At each trial, single samples of strawberry were harvested just before last treatment and at 0, 1, 3/4, 5/6, and 7/8 days after the last treatment.

The strawberry samples were analyzed for residues of the parent compound fluopyram and its metabolites AE C656948-benzamide, AE C656948-PAA, and AE C656948-PCA using an adequate HPLC/MS/MS method, Method No. 00984-M001. The LOQ (expressed as parent equivalents) was 0.01 ppm for all analytes. Sample storage conditions and durations are reported in Table 7; samples were stored frozen for up to ~9 months prior to analysis. The available storage stability data support the strawberry study.

The results of the Europe strawberry greenhouse trials are summarized in Table 19; only data for residues of fluopyram are included. In greenhouse trials, residues of fluopyram at the 1-day PHI ranged from 0.12-0.79 ppm in strawberry fruit (median 0.27 ppm). Residues of the metabolite AE C656948-PAA were <LOQ in/on all samples at all sampling events. Residues of the metabolite AE C656948-PCA were <LOQ in/on all samples at the 1-day PHI. Residues of the metabolite AE C656948-benzamide were <LOQ in/on all samples at all sampling intervals, except for one trial where quantifiable residues were observed at all sampling intervals, and residues at 0.02 ppm at the 1-day PHI were obtained.

Analysis of the data for the different PHIs indicated decline of fluopyram residue levels in/on strawberry fruits with time. The decline in fluopyram residues between first and last sampling days averaged 36% for the trials conducted in greenhouse (excepted in one trial where no decline was observed).

*Conclusions*. The submitted crop field trial data for strawberry are adequate to satisfy data. The number and locations of the North American field trials are in accordance with OPPTS Guideline 860.1500 for strawberry as a representative crop of subgroup 13-07G. Field trials were conducted at ~1x the proposed maximum seasonal rate and samples were harvested at the proposed PHI. The European greenhouse data may be translated to support greenhouse use on strawberries in North America.

Based on the available data and the NAFTA tolerance calculator (see Appendix II), a tolerance of 1.5 ppm for residues of fluopyram in/on strawberry is appropriate.

Sugar beet root

Bayer has submitted magnitude of the residue studies for sugar beet; the results for roots from the sugar beet field trials are discussed below and summarized in Table 20.

| **Table 20. Summary of Residue Data from Sugar Beet Field Trials with Fluopyram.** | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Crop matrix | Total Applic. Rate (lb ai/A) [kg ai/ha] | PHI (days) | Fluopyram Residue Levels (ppm) | | | | | | | |
| | | | n | Min. | Max. | HAFT | Median | Mean | Std. Dev. |
| **SUGAR BEET (proposed use = 0.445 lb ai/A total application rate, 7-day PHI; revised to 0.222 lb ai/A)** | | | | | | | | | | |
| Sugar beet, root | 0.439 – 0.456 (0.492 – 0.511) | 5-7 | 24 | 0.013 | 0.050 | 0.040 | 0.026 | 0.029 | 0.011 |

Twelve trials, representing eleven harvest trials and one decline trial, were conducted in Zones 5 (IL, MN, ND, NE, and WI, 5 trials), 7 (ND, 1 trial), 8 (TX, 1 trial), 9 (ID, 1 trial), 10 (CA, 2 trials), and 11 (ID and OR, 2 trials) during the 2006 growing season.

Two foliar spray applications of the 4.16 lb/gal SC formulation at a rate of 0.216-0.230 lb ai/A/application (242-258 g ai/ha) were made to sugar beet with 5- to 7-day RTIs, for total application rates of 0.439-0.456 lb ai/A (492-511 g ai/ha). The application rates represent ~2x the proposed maximum seasonal rate. Applications were made in spray volumes of 9-22 GPA (80-201 L/ha). Duplicate treated samples of roots were harvested 5-7 days following the last application in the harvest trials, and 0, 6, 13, 19, and 27 days following last application in the decline trial. Samples of sugar beet tops were also collected; these data are discussed below under sugar beet tops.

The sugar beet root samples were analyzed for residues of fluopyram using an adequate HPLC/MS/MS method, Method No. GM-001-P07-01. The LOQ was 0.01 ppm in sugar beet root. Sample storage conditions and durations are reported in Table 7; samples were stored frozen for up to ~19 months prior to analysis. The available storage stability data support the sugar beet field trial study.

The results for roots from the sugar beet field trials are summarized in Table 20. Residues of fluopyram in/on sugar beet roots at a 5- to 7-day PHI ranged from 0.013-0.050 ppm. The mean and HAFT were 0.029 ppm and 0.040 ppm, respectively. In the decline trial, the average residues decreased in/on sugar beet roots from the 0-day PHI to the 27-day PHI.

*Conclusions*. The submitted sugar beet crop field trial data are adequate to fulfill data requirements. The number and locations of the field trials are in accordance with OPPTS Guideline 860.1500 for sugar beets. Field trials were conducted at ~2x the proposed maximum seasonal rate and samples were harvested at the proposed PHI.

The residue data have been adjusted for rate differential and based on the NAFTA tolerance calculator (see Appendix II), a tolerance of 0.04 ppm for residues of fluopyram in/on sugar beet root is appropriate.

Sugar beet tops

Bayer has submitted magnitude of the residue studies for sugar beet and turnip tops, the representative crops of leaves of root and tuber vegetables, group 2, as well as for radish tops. The results from the sugar beet tops field trials are discussed below and summarized in Table 21.

| **Table 21. Summary of Residue Data from Sugar Beet Top Field Trials with Fluopyram.** | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Crop matrix | Total Applic. Rate (lb ai/A) [kg ai/ha] | PHI (days) | Fluopyram Residue Levels (ppm) | | | | | | |
| | | | n | Min. | Max. | HAFT | Median | Mean | Std. Dev. |
| **SUGAR BEET (proposed use = 0.445 lb ai/A total application rate, 7-day PHI; revised to 0.222 lb ai/A)** | | | | | | | | | |
| Sugar beet, tops | 0.439 – 0.456 (0.492 – 0.511) | 5-7 | 24 | 0.273 | 18.7 | 16.5 | 0.803 | 3.30 | 4.89 |

Twelve trials, representing eleven harvest trials and one decline trial, were conducted in Zones 5 (IL, MN, ND, NE, and WI, 5 trials), 7 (ND, 1 trial), 8 (TX, 1 trial), 9 (ID, 1 trial), 10 (CA, 2 trials), and 11 (ID and OR, 2 trials) during the 2006 growing season.

Two foliar spray applications of the 4.16 lb/gal SC formulation at a rate of 0.216-0.230 lb ai/A/application (242-258 g ai/ha) were made to sugar beet with 5- to 7-day RTIs, for total application rates of 0.439-0.456 lb ai/A (492-511 g ai/ha). The application rates represent ~2x the proposed maximum seasonal rate. Applications were made in spray volumes of 9-22 GPA (80-201 L/ha). Duplicate treated samples of tops were harvested 5-7 days following the last application in the harvest trials, and 0, 6, 13, 19, and 27 days following last application in the decline trial.

The sugar beet top samples were analyzed for residues of fluopyram using an adequate HPLC/MS/MS method, Method No. GM-001-P07-01. The LOQ was 0.01 ppm in sugar beet tops. Sample storage conditions and durations are reported in Table 7; samples were stored frozen for up to ~19 months prior to analysis. The available storage stability data support the sugar beet field trial study.

The results for tops from the sugar beet field trials are summarized in Table 21. Residues of fluopyram in/on sugar beet tops at a 5- to 7-day PHI ranged from 0.27-18.7 ppm. The mean and HAFT were 3.30 ppm and 16.5 ppm, respectively. In the decline trial, the average residues decreased in/on sugar beet tops from the 0-day PHI to the 27-day PHI.

*Conclusions*. The submitted sugar beet crop field trial data are adequate to fulfill data requirements. The number and locations of the field trials are in accordance with OPPTS Guideline 860.1500 for leaves of sugar beet. Field trials for sugar beet were conducted at ~2x the proposed maximum seasonal rate and samples were harvested at the proposed PHI.

Sugar beet tops are no longer considered a livestock feed item. Therefore, a tolerance for residues of fluopyram in/on leaves of sugar beet is not needed.

Cucurbit vegetable, group 9

Bayer has submitted magnitude of the residue studies for cucumber, melon, and summer squash, the representative crops of cucurbit vegetable, group 9. The results from these field trials are discussed below and summarized in Table 22. *Per letter of 8 August 2011, the registrant withdrew use on the cucurbit crop group and instead proposed use on watermelon only.*

**Table 22. Summary of Residue Data from Crop Group 9 Field Trials with Fluopyram.**

| Crop matrix | Total Applic. Rate (lb ai/A) [kg ai/ha] | PHI (days) | Fluopyram Residue Levels (ppm) | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | n | Min. | Max. | HAFT | Median | Mean | Std. Dev. |
| **CUCURBIT VEGETABLES (proposed use = 0.445 lb ai/A total application rate, 0-day PHI spray uses, 3-day PHI greenhouse uses, and 7-day PHI drip applications)** | | | | | | | | | |
| **Foliar Spray Applications** | | | | | | | | | |
| Cucumber | 0.432-0.454 (0.485-0.508) | 0 | 12 | 0.037 | 0.189 | 0.144 | 0.092 | 0.094 | 0.045 |
| Muskmelon | 0.445-0.469 (0.499-0.526) | 0 | 12 | 0.069 | 0.529 | 0.439 | 0.192 | 0.217 | 0.156 |
| Summer squash | 0.443-0.445 (0.497-0.510) | 0 | 10 | 0.0468 | 0.179 | 0.173 | 0.083 | 0.099 | 0.047 |
| **Drip Line Irrigation** | | | | | | | | | |
| Cucumber | 0.446-0.456 (0.500-0.511) | 7 | 12 | <0.01 | 0.058 | 0.057 | 0.016 | 0.022 | 0.017 |
| Muskmelon | 0.446-0.455 (0.500-0.510) | 5-7 | 12 | <0.01 | 0.029 | 0.027 | <0.01 | 0.015 | 0.008 |
| Summer squash | 0.446 (0.500) | 6-7 | 10 | <0.01 | 0.017 | 0.015 | 0.013 | 0.012 | 0.002 |
| **Greenhouse Applications** | | | | | | | | | |
| Cucumber (European data) | 0.535 (0.600) | 2-4 | 8 | 0.04 | 0.29 | 0.29 | 0.12 | 0.15 | 0.09 |
| Muskmelon (European data) | 0.535 (0.600) | 3[1] | 7 | 0.04 | 0.19 | 0.19 | 0.11 | 0.12 | 0.05 |

[1] The data include results from one trial with a PHI of 1 day (no sample collected at 3-day PHI) and one trial with a PHI of 7 days (residues were higher than those at the 3-day PHI).

Cucumber

Six cucumber trials, representing five harvest trials and one decline trial, were conducted in Zones 2 (GA and NC, 2 trials), 3 (FL, 1 trial), 5 (IA and OH, 2 trials), and 6 (TX, 1 trial) during the 2007 growing season.

At each trial site there was one untreated plot and two treated plots. At one treated plot, two foliar spray applications of the 4.16 lb/gal SC formulation at a rate of 0.210-0.229 lb ai/A (235-257 g ai/ha) were made to cucumber with a 5- to 6-day application interval, for total application rates of 0.432-0.454 lb ai/A (485-508 g ai/ha). The foliar spray application rates represent ~1x the proposed maximum seasonal rate. Foliar spray applications were made in spray volumes of 16-19 GPA (146-182 L/ha). Duplicate treated samples were harvested on the day of last application in the foliar spray harvest trials, and 0, 1, 3, 7, and 10 days following the final application in the foliar spray decline trial.

At the other treated plot, two drip line irrigation applications of the 4.16 lb/gal SC formulation at a rate of 0.223-0.233 lb ai/A (250-261 g ai/ha) were made to cucumber with a 5- to 6-day application interval, for total application rates of 0.446-0.456 lb ai/A (500-511 g ai/ha). The drip line irrigation application rates represent ~1x the proposed maximum seasonal rate. Drip line irrigation applications were made in spray volumes of 0.12-0.57 gal/hr (0.47-2.2 L/hr). Duplicate samples of cucumber were harvested at a 7-day PHI in the drip line irrigation harvest trials, and 0, 3, 7, 10, and 14 days following the final application for the drip line irrigation decline trial.

The cucumber samples were analyzed for residues of fluopyram using an adequate HPLC/MS/MS method, Method No. GM-001-P07-01. The LOQ was 0.01 ppm in cucumber fruit. Sample storage conditions and durations are reported in Table 7; samples were stored frozen for up to ~9 months prior to analysis. The available storage stability data support the cucumber field trial study.

The results of the cucumber field trials are summarized in Table 22. Residues of fluopyram in/on cucumber fruit at a 0-day PHI for the plots with foliar spray applications ranged from 0.037-0.19 ppm. The mean and HAFT were 0.094 ppm and 0.14 ppm, respectively. Residues of fluopyram in/on cucumber fruit at a 7-day PHI for the plots with drip line irrigation applications ranged from <0.01-0.058 ppm. The mean and HAFT were 0.02 ppm and 0.057 ppm, respectively. In the decline trial with foliar spray applications, a more than 50% reduction of residue levels was observed from the 0-day to the 10-day PHI. In the decline trial with drip line irrigation, no major increase or decrease of residues was observed from the 0-day PHI to the 14-day PHI for cucumber fruit samples.

<u>Europe</u>: Eight greenhouse trials on cucumber were conducted during the 2006 growing season according to the critical European GAP. The greenhouse trials were located in southern France (2), Spain, Italy, Germany (2), Netherlands, and Greece. The results reported herein were obtained from "Tier 2 Summary of the Metabolism and Residues Data for Fluopyram (AE C656948)," which was prepared by Bayer CropScience (MRID 47567126).

In the greenhouse trials, the 4.16 lb/gal SC formulation was applied as sprays twice with an application rate of 0.6 L/ha and 750-1500 L water per ha, corresponding to a spray concentration of 0.04 to 0.08% and a rate of 0.30 kg ai/ha/application. All applications were made at the specified rates. Total application rates were 0.600 kg ai/ha (0.535 lb ai/A) for the greenhouse trials, representing ~1.2x the proposed maximum seasonal rate.

The applications were carried out with 6- to 7-day RTIs with the last application approximately 1 day prior to the expected date of harvest. At each trial, single samples of cucumber were harvested just before last treatment and at 0, 1, 2/3/4, 5, and 7 days after the last treatment.

The cucumber samples were analyzed for residues of the parent compound fluopyram and its metabolites AE C656948-benzamide, AE C656948-PAA, and AE C656948-PCA using an adequate HPLC/MS/MS method, Method No. 00984. The LOQ (expressed as parent equivalents) was 0.01 ppm for all analytes. Sample storage conditions and durations are reported in Table 7; samples were stored frozen for up to ~11 months prior to analysis. The available storage stability data support the cucumber field trial study.

The results of the Europe cucumber greenhouse trials are summarized in Table 22, reflecting residues of fluopyram only and the desired 3-day PHI. In greenhouse, the residues of fluopyram at a 2- to 4-day PHI ranged from 0.04-0.29 ppm in cucumber fruit (median 0.12 ppm). Residues of the three metabolites AE C656948-PAA, AE C656948-benzamide, and AE C656948-PCA were <LOQ in/on all samples at all sampling events.

Analysis of the data for the different PHIs indicated decline of fluopyram residue levels in/on cucumber fruits with time. The decline in fluopyram residues between first and last sampling day averaged 46%.

Melon

Six muskmelon trials, representing five harvest trials and one decline trial, were conducted in Zones 2 (GA, 1 trial), 5 (ND, 1 trial), 6 (TX, 1 trial), and 10 (CA, 3 trials) during the 2007 growing season.

At each trial site there was one untreated plot and two treated plots. At one treated plot, two foliar spray applications of the 4.16 lb/gal SC formulation at a rate of 0.220-0.235 lb ai/A (246-263 g ai/ha) were made to melon with a 5-day application interval, for total application rates of 0.445-0.469 lb ai/A (499-526 g ai/ha). The foliar spray application rates represent ~1x the proposed maximum seasonal rate. Foliar spray applications were made in spray volumes of 15-18 GPA (139-172 L/ha). Duplicate treated samples were harvested on the day of last application in the foliar spray harvest trials, and 0, 1, 3, 7, and 10 days following the final application in the foliar spray decline trial.

At the other treated plot, two drip line irrigation applications of the 4.16 lb/gal SC formulation at a rate of 0.223-0.228 lb ai/A (250-255 g ai/ha) were made to muskmelon with a 5-day application interval, for total application rates of 0.446-0.455 lb ai/A (500-510 g ai/ha). The drip line irrigation application rates represent ~1x the proposed maximum seasonal rate. Drip line irrigation applications were made in spray volumes of 0.23-0.43 gal/hr (0.88-1.6 L/hr). Duplicate samples of muskmelon were harvested at a 5- to 7-day PHI in the drip line irrigation harvest trials, and 0, 3, 7, 10, and 14 days following the final application for the drip line irrigation decline trial.

The muskmelon samples were analyzed for residues of fluopyram using an adequate HPLC/MS/MS method, Method No. GM-001-P07-01. The LOQ was 0.01 ppm in muskmelon fruit. Sample storage conditions and durations are reported in Table 7; samples were stored frozen for up to ~7 months prior to analysis. The available storage stability data support the muskmelon field trial study.

The results of the muskmelon field trials are summarized in Table 22. Residues of fluopyram in/on muskmelon fruit at a 0-day PHI for the plots with foliar spray applications ranged from 0.069-0.53 ppm. The mean and HAFT were 0.22 ppm and 0.44 ppm, respectively. Residues of fluopyram in/on muskmelon fruit at a 5- to 7-day PHI for the plots with drip line irrigation applications ranged from <0.01-0.029 ppm. The mean and HAFT were 0.015 ppm and 0.027 ppm, respectively. In the decline trial with foliar spray applications, residues increased from the 0-day PHI to the 1-day PHI, and then did not increase from the 3- to the 10-day PHI. Residues were <0.01 ppm in/on all samples from the decline trial for drip line irrigation treatment.

Europe: Seven greenhouse trials on melon/watermelon were conducted during the 2006 and 2007 growing seasons according to the critical European GAP. The greenhouse trials were located in southern France (2), Spain (2), Italy, Germany, and Portugal. The results reported herein were obtained from "Tier 2 Summary of the Metabolism and Residues Data for Fluopyram (AE C656948)," which was prepared by Bayer CropScience (MRID 47567126). In the greenhouse trials, the 4.16 lb/gal SC formulation was applied as sprays twice with an application rate of 0.6 L/ha and 600-1000 L water per ha, corresponding to a spray concentration of 0.06-0.1% and 0.30 kg ai/ha/application. All applications were made at the specified rates. Total application rates were 0.600 kg ai/ha (0.535 lb ai/A) for the greenhouse trials, representing ~1.2x the proposed maximum seasonal rate.

The applications were carried out with 7-day RTIs with the last application approximately 3 days prior to the expected date of harvest. At each trial, single samples of melon were harvested just before last treatment and at 0, 1, 3, and 7 days after the last treatment.

The melon samples were analyzed for residues of the parent compound fluopyram and its metabolites AE C656948-benzamide, AE C656948-PAA, and AE C656948-PCA using an adequate HPLC/MS/MS method, Method No. 00984. The LOQ (expressed as parent equivalents) was 0.01 ppm for all analytes. Sample storage conditions and durations are reported in Table 7; samples were stored frozen for up to ~10 months prior to analysis. The available storage stability data support the melon field trial study.

The results of the Europe melon greenhouse trials are summarized in Table 22, reflecting residues of fluopyram only and the desired 3-day PHI. In greenhouse, the residues of fluopyram at a 3-day PHI ranged from 0.04 and 0.19 ppm (which includes one trial at 0.04 ppm at day 7 and one trial at 0.09 ppm at day 1) in melon fruit (median 0.11 ppm). Residues of the three metabolites AE C656948-PAA, AE C656948-benzamide, and AE C656948-PCA were <LOQ in/on all samples at all sampling events.

Analysis of the data for the different PHIs indicated decline of fluopyram residue levels in/on melon/watermelon fruits with time. The decline in fluopyram residues between first and last sampling days averaged 52% for 6 greenhouse trials; for one other greenhouse trial, no decline was observed.

Squash

Five summer squash trials, representing four harvest trials and one decline trial, were conducted in Zones 1 (PA, 1 trial), 2 (GA, 1 trial), 3 (FL, 1 trial), 5 (WI, 1 trial), and 10 (CA, 1 trial) during the 2007 growing season.

At each trial site there was one untreated plot and two treated plots. At one treated plot, two foliar spray applications of the 4.16 lb/gal SC formulation at a rate of 0.221-0.229 lb ai/A (248-257 g ai/ha) were made to summer squash with a 5-day application interval, for total application rates of 0.443-0.455 lb ai/A (497-510 g ai/ha). The foliar spray application rates represent ~1x the proposed maximum seasonal rate. Foliar spray applications were made in spray volumes of 14-20 GPA (131-187 L/ha). Duplicate treated samples were harvested on the day of last application in the foliar spray harvest trials, and 0, 1, 3, 7, and 10 days following the final application for the foliar spray decline trial.

At the other treated plot, two drip line irrigation applications of the 4.16 lb/gal SC formulation at a rate of 0.223 lb ai/A (250 g ai/ha) were made to summer squash with a 5-day application interval, for total application rates of 0.446 lb ai/A (500 g ai/ha). The drip line irrigation application rates represent ~1x the proposed maximum seasonal rate. Drip line irrigation applications were made in spray volumes of 0.16-0.47 gal/hr (0.61-1.8 L/hr). Duplicate samples of summer squash were harvested at a 6- to 7-day PHI in the drip line irrigation harvest trials, and 0, 3, 7, 10, and 14 days following the final application in the drip line irrigation decline trial.

The squash samples were analyzed for residues of fluopyram using an adequate HPLC/MS/MS method, Method No. GM-001-P07-01. The LOQ was 0.01 ppm in summer squash fruit. Sample storage conditions and durations are reported in Table 7; samples were stored frozen for up to ~9 months prior to analysis. The available storage stability data support the summer squash field trial study.

The results of the summer squash field trials are summarized in Table 22. Residues of fluopyram in/on summer squash fruit at a 0-day PHI for the plots with foliar spray applications ranged from 0.047-0.18 ppm. The mean and HAFT were 0.10 ppm and 0.17 ppm, respectively. Residues of fluopyram in/on summer squash fruit at a 6- to 7-day PHI for the plots with drip line irrigation applications ranged from <0.01-0.017 ppm. The mean and HAFT were 0.012 ppm and 0.015 ppm, respectively. In the decline trial with foliar spray applications, residues increased from the 0-day PHI to the 1-day PHI, and then decreased to <0.01 ppm at the 10-day PHI. For the drip line irrigation decline trial, residues increased from <0.01 ppm at the 0-day PHI to 0.017 ppm at the 14-day PHI.

*Conclusions*. The submitted residue data for cucumber, muskmelon, and summer squash are adequate to fulfill data requirements. The number and locations of the field trials are in accordance with OPPTS Guideline 860.1500 for cucurbit vegetables, group 9. Field trials were conducted at ~1x the proposed maximum seasonal rate and samples were harvested at the proposed PHIs for each application type. The residue data for muskmelon are applicable to watermelon.

Based on the available data and the NAFTA tolerance calculator (see Appendix II), a tolerance of 1.0 ppm for residues of fluopyram in/on watermelon is appropriate.

Stone fruit, group 12

Bayer has submitted magnitude of the residue studies for peach, cherry, and plum, the representative crops of stone fruit, group 12. The results from these field trials are discussed below and summarized in Table 23. *Per letter of 8 August 2011, the registrant withdrew uses on stone fruit group 12 and instead petitioned use on cherry only.*

| **Table 23. Summary of Residue Data from Crop Group 12 Field Trials with Fluopyram.** | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Crop matrix | Total Applic. Rate (lb ai/A) [kg ai/ha] | PHI (days) | Fluopyram Residue Levels (ppm) | | | | | | |
| | | | n | Min. | Max. | HAFT | Median | Mean | Std. Dev. |
| **STONE FRUIT (proposed use = 0.445 lb ai/A total application rate, 0-day PHI; revised cherry use = 0.183 lb ai/A, revised stone fruit use other than cherry = 0.367 lb ai/A)** | | | | | | | | | |
| **Concentrate Spray** | | | | | | | | | |
| Cherry | 0.447 – 0.460 (0.501 – 0.516) | 0 | 12 | 0.066 | 0.641 | 0.639 | 0.505 | 0.425 | 0.223 |
| Peach | 0.436 – 0.456 (0.489 – 0.511) | 0 | 18 | 0.126 | 0.457 | 0.44 | 0.306 | 0.29 | 0.105 |
| Plum | 0.429 – 0.445 (0.481 – 0.499) | 0 | 12 | 0.022 | 0.286 | 0.257 | 0.052 | 0.082 | 0.085 |
| **Dilute Spray** | | | | | | | | | |
| Cherry | 0.444 – 0.457 (0.498 – 0.512) | 0 | 12 | 0.147 | 1.229 | 1.174 | 0.396 | 0.516 | 0.349 |
| Peach | 0.441 – 0.457 (0.494 – 0.512) | 0 | 18 | 0.175 | 0.588 | 0.548 | 0.318 | 0.34 | 0.121 |
| Plum | 0.442 – 0.454 (0.495 – 0.509) | 0 | 12 | 0.021 | 0.292 | 0.283 | 0.044 | 0.083 | 0.095 |

Cherry

Six cherry (sweet and tart) trials, representing five harvest trials and one decline trial, were conducted during the 2006 growing season. Four sweet cherry trials were conducted in Zones 5 (MI, 1 trial), 10 (CA, 1 trial), and 11 (OR and WA, 2 trials). Two tart cherry trials were conducted in Zones 1 (PA, 1 trial) and 5 (MI, 1 trial).

At each trial site there was one untreated plot and two treated plots. At each treated plot, two foliar spray applications of the 4.16 lb/gal SC formulation at a rate of 0.219-0.231 lb ai/A (245-259 g ai/ha) were made to cherries with a 5- to 8-day application interval, for total application rates of 0.444-0.460 lb ai/A (498-516 g ai/ha). The foliar spray application rates represent ~2.4x the proposed maximum seasonal rate. Foliar spray applications were made in concentrate spray volumes, 45-67 GPA (419-624 L/ha), at one treated plot and in dilute spray volumes, 204-309 GPA (1905-2889 L/ha), at the other treated plot. Duplicate treated samples were harvested on the day of the last application in the harvest trials and 0, 3, 7, 10, and 14 days following the last application in the decline trial.

The cherry fruit samples were analyzed for residues of fluopyram using an adequate HPLC/MS/MS method, Method No. GM-001-P07-01. The LOQ was 0.01 ppm in cherries. Sample storage conditions and durations are reported in Table 7; samples were stored frozen for up to ~18 months prior to analysis. The available storage stability data support the cherry field trial study.

The results of the cherry field trials are summarized in Table 23. Residues of fluopyram in/on cherry fruit at a 0-day PHI for the plots with concentrate spray volumes ranged from 0.066-0.64 ppm. The mean and HAFT were 0.43 ppm and 0.64 ppm, respectively. Residues of fluopyram in/on cherry fruit at a 0-day PHI for the plots with dilute spray volumes ranged from 0.15-1.23

ppm. The mean and HAFT were 0.52 ppm and 1.17 ppm, respectively. In the decline trial, average residues decreased between the 0- and the 14-day PHI.

Peach

Nine peach trials, representing eight harvest trials and one decline trial, were conducted in Zones 1 (PA, 1 trial), 2 (GA, 3 trials), 5 (MI, 1 trial), 6 (TX, 1 trial), and 10 (CA, 3 trials) during the 2006 and 2007 growing seasons.

At each trial site there was one untreated plot and two treated plots. At each treated plot, two foliar spray applications of the 4.16 lb/gal SC formulation at a rate of 0.213-0.233 lb ai/A (239-261 g ai/ha) were made to peaches with a 5- to 7-day application interval, for total application rates of 0.436-0.457 lb ai/A (489-512 g ai/ha). The foliar spray application rates represent ~1.2x the proposed maximum seasonal rate. Foliar spray applications were made in concentrate spray volumes, 40-62 GPA (371-577 L/ha), at one treated plot and in dilute spray volumes, 210-358 GPA (1962-3350 L/ha), at the other treated plot. Duplicate treated samples were harvested on the day of the last application in the harvest trials and 0, 3, 7, 10, and 14 days following the last application in the decline trial.

The peach fruit samples were analyzed for residues of fluopyram using an adequate HPLC/MS/MS method, Method No. GM-001-P07-01. The LOQ was 0.01 ppm in peaches. Sample storage conditions and durations are reported in Table 7; samples were stored frozen for up to ~18 months prior to analysis. The available storage stability data support the peach field trial study.

The results of the peach field trials are summarized in Table 23. Residues of fluopyram in/on peach fruit at a 0-day PHI for the plots with concentrate spray volumes ranged from 0.13-0.46 ppm. The mean and HAFT were 0.29 ppm and 0.44 ppm, respectively. Residues of fluopyram in/on peach fruit at a 0-day PHI for the plots with dilute spray volumes ranged from 0.18-0.59 ppm. The mean and HAFT were 0.34 ppm and 0.55 ppm, respectively. In the decline trial, average residues remained approximately the same from the 0-day PHI to the 14-day PHI.

Plum

Six plum trials, representing five harvest trials and one decline trial, were conducted in Zones 5 (MI, 1 trial), 10 (CA, 4 trials), and 12 (OR, 1 trial) during the 2006 growing season.

At each trial site there was one untreated plot and two treated plots. At each treated plot, two foliar spray applications of the 4.16 lb/gal SC formulation at a rate of 0.213-0.227 lb ai/A (239-254 g ai/ha) were made to plums with a 6- to 7-day application interval, for total application rates of 0.429-0.454 lb ai/A (481-509 g ai/ha). The foliar spray application rates represent ~1.2x the proposed maximum seasonal rate. Foliar spray applications were made in concentrate spray volumes, 43-61 GPA (405-574 L/ha), at one treated plot and in dilute spray volumes, 206-303 GPA (1923-2853 L/ha), at the other treated plot. Duplicate treated samples were harvested on the day of the last application in the harvest trials and 0, 3, 7, 10, and 14 days following the last application in the decline trial.

The plum fruit samples were analyzed for residues of fluopyram using an adequate HPLC/MS/MS method, Method No. GM-001-P07-01. The LOQ was 0.01 ppm in plums.

Sample storage conditions and durations are reported in Table 7; samples were stored frozen for up to ~18 months prior to analysis. The available storage stability data support the plum field trial study.

The results of the plum field trials are summarized in Table 23. Residues of fluopyram in/on plum fruit at a 0-day PHI for the plots with concentrate spray volumes ranged from 0.02-0.29 ppm. The mean and HAFT were 0.082 ppm and 0.26 ppm, respectively. Residues of fluopyram in/on plum fruit at a 0-day PHI for the plots with dilute spray volumes ranged from 0.021-0.29 ppm. The mean and HAFT were 0.083 ppm and 0.28 ppm, respectively. In the decline trial, average residues increased from the 0-day to 7-day PHI and then decreased from the 7-day to the 14-day PHI.

*Conclusions*. The submitted residue data for peach and plum are adequate to fulfill data requirements. The number and locations of the field trials are in accordance with OPPTS Guideline 860.1500 for stone fruit, group 12. Field trials were conducted at ~1.2x (within 25% of) the proposed maximum seasonal rate and samples were harvested at the proposed PHI. The available data support tolerances of 0.70 ppm for residues of fluopyram in/on peach and 0.35 ppm in/on plum.

For cherry, the residue data have been adjusted for rate differential. Based on the available data and the NAFTA tolerance calculator (see Appendix II), a tolerance of 0.60 ppm for residues of fluopyram in/on cherry is appropriate.

Tree nut, group 14

Bayer has submitted magnitude of the residue studies for almond and pecan, the representative crops of tree nuts, group 14. The results from these field trials are discussed below and summarized in Table 24. The results for almond and pecan are also intended to support use on pistachio.

**Table 24. Summary of Residue Data from Crop Group 14 Field Trials with Fluopyram.**

| Crop matrix | Total Applic. Rate (lb ai/A) [kg ai/ha] | PHI (days) | Fluopyram Residue Levels (ppm) | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | n | Min. | Max. | HAFT | Median | Mean | Std. Dev. |
| **TREE NUT (proposed use = 0.445 lb ai/A total application rate, 14-day PHI)** | | | | | | | | | |
| **Concentrate Spray** | | | | | | | | | |
| Almond | 0.437-0.449 (0.490-0.503) | 14 | 10 | <0.01 | 0.019 | 0.018 | <0.01 | 0.01 | 0.01 |
| Almond, hulls | 0.437-0.449 (0.490-0.503) | 14 | 10 | 1.93 | 4.45 | 4.25 | 3.26 | 3.18 | 1.09 |
| Pecan | 0.445-0.455 (0.499-0.510) | 12-14 | 10 | <0.01 | 0.021 | 0.018 | <0.01 | 0.01 | 0.01 |
| **Dilute Spray** | | | | | | | | | |
| Almond | 0.439- 0.462 (0.492-0.518) | 14 | 10 | <0.01 | 0.016 | 0.015 | <0.01 | 0.01 | 0.01 |
| Almond, hulls | 0.439- 0.462 (0.492-0.518) | 14 | 10 | 1.22 | 6.12 | 5.43 | 2.44 | 2.97 | 1.57 |
| Pecan | 0.448-.458 (0.502-0.513) | 12-14 | 10 | <0.01 | 0.045 | 0.031 | <0.01 | 0.01 | 0.014 |

Almond

Five almond trials, representing four harvest trials and one decline trial, were conducted in Zone 10 (CA) during the 2006 growing season.

At each trial site there was one untreated plot and two treated plots. At each treated plot, two foliar spray applications of the 4.16 lb/gal SC formulation at a rate of 0.218-0.231 lb ai/A (244-259 g ai/ha) were made to almonds with a 6- to 7-day application interval, for total application rates of 0.437-0.462 lb ai/A (490-518 g ai/ha). The foliar spray application rates represent ~1x the proposed maximum seasonal rate. Foliar spray applications were made in concentrate spray volumes, 50-60 GPA (468-561 L/ha), at one treated plot and in dilute spray volumes, 209-299 GPA (1956-2799 L/ha), at the other treated plot. Duplicate treated samples (nutmeat and hulls) were harvested 14 days after the last application in the harvest trials. Additionally, samples were collected from one plot at 0, 7, 14, 21, and 28 days following the final application in the decline trial.

The almond samples (nutmeat and hulls) were analyzed for residues of fluopyram using an adequate HPLC/MS/MS method, Method No. GM-001-P07-01. The LOQ was 0.01 ppm in almond hulls and nutmeat. Sample storage conditions and durations are reported in Table 7; samples were stored frozen for up to ~22 months prior to analysis. The available storage stability data support the almond field trial study.

The results of the almond field trials are summarized in Table 24. Residues of fluopyram in/on almond hulls at a 14-day PHI for the plots with concentrate spray volumes ranged from 1.93-4.45 ppm. The mean and HAFT were 3.18 ppm and 4.25 ppm, respectively. Residues of fluopyram in/on almond hulls at a 14-day PHI for the plots with dilute spray volumes ranged from 1.22-6.12 ppm. The mean and HAFT were 2.97 ppm and 5.43 ppm, respectively. In the decline trial, average residues in the almond hulls decreased from the 0-day PHI to the 7-day PHI, then increased from the 7-day PHI to the 28-day PHI (noted dry matter content also increased in longer PHI samples).

Residues of fluopyram in/on almond nutmeat at a 14-day PHI for the plots with concentrate spray volumes ranged from <0.01-0.019 ppm. The mean and HAFT were 0.01 ppm and 0.018 ppm, respectively. Residues of fluopyram in/on almond nutmeat at a 14-day PHI for the plots with dilute spray volumes ranged from <0.01-0.016 ppm. The mean and HAFT were 0.01 ppm and 0.015 ppm, respectively. In the decline trial, average residues in the almond nutmeat increased from the 0-day PHI to the 14-day PHI, and then declined from the 21-day PHI to the 28-day PHI.

Pecan

Five pecan trials, representing four harvest trials and one decline trial, were conducted in Zones 2 (GA, 2 trials), 4 (AR, 1 trial), 6 (TX, 1 trial), and 8 (TX, 1 trial) during the 2006 growing season.

At each trial site there was one untreated plot and two treated plots. At each treated plot, two foliar spray applications of the 4.16 lb/gal SC formulation at a rate of 0.219-0.232 lb ai/A (246-260 g ai/ha) were made to pecans with a 13- to 14-day application interval, for total application rates of 0.445-0.458 lb ai/A (499-513 g ai/ha). The foliar spray application rates represent ~1x the proposed maximum seasonal rate. Foliar spray applications were made in concentrate spray volumes, 41-69 GPA (385-647 L/ha), at one treated plot and in dilute spray volumes, 205-308 GPA (1914-2879 L/ha), at the other treated plot. Duplicate treated samples (nutmeat) were harvested 12-14 days after the last application in the harvest trials and 0, 7, 14, 21, and 28 days following the last application in the decline trial.

The pecan samples (nutmeat) were analyzed for residues of fluopyram using an adequate HPLC/MS/MS method, Method No. GM-001-P07-01. The LOQ was 0.01 ppm in pecan nutmeat. Sample storage conditions and durations are reported in Table 7; samples were stored frozen for up to ~19 months prior to analysis. The available storage stability data support the pecan field trial study.

The results of the pecan field trials are summarized in Table 24. Residues of fluopyram in/on pecan nutmeat at a 12- to 14-day PHI for the plots with concentrate spray volumes ranged from <0.01-0.021 ppm. The mean and HAFT were 0.01 ppm and 0.018 ppm, respectively. Residues of fluopyram in/on pecan nutmeat at a 12- to 14-day PHI for the plots with dilute spray volumes ranged from <0.01-0.045 ppm. The mean and HAFT were 0.01 ppm and 0.031 ppm, respectively. In the decline trial, average residues in the pecan nutmeat decreased from the 0-day PHI to <0.01 ppm at the 14-day PHI and remained <LOQ to the 28-day PHI.

*Conclusions*. The submitted residue data for almond and pecan are adequate to fulfill data requirements. The number and locations of the field trials are in accordance with OPPTS Guideline 860.1500 for tree nut, group 14. Field trials were conducted at ~1x the proposed maximum seasonal rate and samples were harvested at the proposed PHI.

Based on the available data and the NAFTA tolerance calculator (see Appendix II), a tolerance of 0.05 ppm for residues of fluopyram in/on tree nut, group 14 and a tolerance of 8.0 ppm for residues of fluopyram in/on almond hulls are appropriate.

Banana

Bayer has submitted magnitude of the residue studies for banana. The results from these field trials are discussed below and summarized in Table 25.

**Table 25. Summary of Residue Data from Banana Field Trials with Fluopyram.**

| Crop matrix | Total Applic. Rate [kg ai/ha] | PHI (days) | Fluopyram Residue Levels (ppm) | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | n | Min. | Max. | HAFT | Median | Mean | Std. Dev. |
| **BANANA - Latin America (no proposed use information was provided for banana)** | | | | | | | | | |
| Banana, whole fruit, bagged | 0.587-0624 | 0 | 28 | <0.01 | 0.040 | 0.038 | 0.015 | 0.018 | 0.009 |
| Banana, whole fruit, unbagged | 0.587-0624 | 0 | 28 | 0.018 | 0.526 | 0.510 | 0.144 | 0.164 | 0.140 |

Fourteen banana trials, representing twelve harvest trials and two decline trials, were conducted in Costa Rica (4 trials), Ecuador (4 trials), Guatemala (2 trials), Honduras (1 trial), Mexico (1 trial), and Colombia (2 trials) during the 2007 growing season.

Six foliar spray applications of the 4.16 lb/gal SC formulation at a rate of 0.0803-0.0999 lb ai/A/application (90-112 g ai/ha) were made to bananas with 5- to 11-day RTIs, for total application rates of 0.524 to 0.557 lb ai/A (587 to 624 g ai/ha). Applications were made to unbagged and bagged bananas; bagged bananas had a perforated plastic bag placed over the fruit at the normal time the bagging operation is commercially performed, approximately one week after flowering begins. The target application pattern was six application at 0.0892 lb ai/A/application (0.100 kg ai/ha/application) with a 7-day RTI. The petitioner did not provide any information pertaining to the proposed use of fluopyram on bananas. Applications were made in spray volumes of 2.25-6.73 GPA (21-63 L/ha). Duplicate treated samples of banana (bagged and unbagged) were harvested on the day of last application in the harvest trials, and 0, 2/3, 5, and 6/7 days following last application in the decline trials (unbagged bananas only).

The banana samples were analyzed for residues of fluopyram using an adequate HPLC/MS/MS method, Method No. GM-001-P07-01. The LOQ was 0.01 ppm in/on banana. For residues of the metabolites AE C656948-benzamide, AE C656948-PAA, and AE C656948-PCA, extracts were diluted with appropriate solvents and analyzed by HPLC/MS/MS. The method was adequate for data collection based on acceptable concurrent method recoveries. The LOQ was 0.01 ppm for each analyte in banana. Sample storage conditions and durations are reported in Table 7; samples were stored frozen for up to ~11 months prior to analysis. The available storage stability data support the banana field trial study.

The results of the Latin American banana field trials are summarized in Table 25. Residues of fluopyram in/on bagged whole banana at a 0-day PHI ranged from <0.01-0.040 ppm. The mean and HAFT were 0.018 ppm and 0.038 ppm, respectively. Residues of fluopyram in/on unbagged whole banana at a 0-day PHI ranged from 0.018-0.526 ppm. The mean and HAFT were 0.164 ppm and 0.51 ppm, respectively. No residues of AE C656948-benzamide, AE C656948-PCA or AE C656948-PAA greater than the LOQ of 0.01 ppm were observed in/on whole banana samples treated with fluopyram.

Fluopyram residues declined moderately from the 0- to the 6- to 7-day PHI in unbagged bananas. Placing a perforated plastic bag over the bananas prior to making the fluopyram applications reduced the fluopyram residue significantly, from a mean of 0.164 ppm to a mean of 0.018 ppm.

*Conclusions*. The submitted banana crop field trial data are adequate to fulfill data requirements pending submission of the proposed use directions for banana.

The number and locations of banana field trials conducted in Latin America satisfies the HED geographic representation requirements for an import tolerance on banana. As specified in the "NAFTA Guidance Document on Data Requirements for Tolerances on Imported Commodities in the United States and Canada," a total of 12 field trials are required to support an import tolerance on bananas (amount available for consumption that is imported is >75%, and the maximum percent of diet for banana is between 0.2 and 1.0%). Based on import data from 2003-2007, the major banana importing countries are Guatemala (29.0% of imports), Ecuador (27.4%), Costa Rica (26.9%), Honduras (13.3%), and Colombia (13.3%; data from "Fruit and Tree Nuts Situation and Outlook Yearbook," USDA, 2008).

Based on the available data and the NAFTA tolerance calculator (see Appendix II), a tolerance of 1.0 ppm for residues of fluopyram in/on banana is appropriate.

## 860.1520 Processed Food and Feed

First Entry Monograph for Fluopyram, Sections B.7.7.2.1 through B7.7.2.3 (MRIDs 47372605, 47372622 through 47372630)
Second Entry Monograph for Fluopyram, Sections B.7.7.2.4 through 7.7.2.21 (MRIDs 47567023, 47567025, 47567026, 47567030, and 47567111-47567122)

The residue program in North America included studies to determine levels of fluopyram in processed commodities of apples, canola, corn (field), cotton (rotated), grapes, oranges, peanuts, plums, potatoes, soybeans, sugar beets, sunflowers, tomatoes, and wheat. In addition, the effects of common industrial processes, such as washing, cooking, peeling, canning, and drying, on the reduction of residue levels in many commodities were also investigated.

Bayer submitted processing study data from various processing and residue reduction studies conducted in North America and Europe. Only the North American studies are summarized below. A summary of the average processing factors found for the processed commodities of apple, canola, field corn, cotton (rotated), grape, melon, peanut, plum, potato, soybean, strawberry, sugar beet, and wheat is presented in Table 26.

**Table 26. Summary of Processing Factors for Fluopyram.**

| RAC | Processed Commodity | Average Processing Factor |
|---|---|---|
| Apple | Wet pomace | 2.3 |
| | Juice | 0.4 |
| | Washed fruit | 0.7 |
| | Peeled fruit | 0.03 |
| | Applesauce | 0.01 |
| | Dried fruit | 0.03 |
| Canola | Meal | 0.3 |
| | Refined oil | 0.01 |
| Corn, field | Aspirated grain fractions | 161 |
| | Starch | 0.2 |
| | Refined/bleached/deodorized oil (wet milled) | 0.6 |
| | Grits | 0.5 |
| | Flour | 0.9 |
| | Meal | 0.8 |
| | Bran | 2.6 |
| | Refined/bleached/deodorized oil (dry milled) | 0.1 |
| Cotton (rotated) | Meal | NC[1] |
| | Hulls | NC |
| | Refined oil | NC |
| Melon | Peeled (foliar treatment) | 0.044 |
| | Peeled (drip irrigation) | 0.71 |
| Peanut | Meal | 0.2 |
| | Refined oil | 0.2 |
| | Dry roasted peanuts | 0.3 |
| | Peanut butter | 0.2 |

| **Table 26.** | **Summary of Processing Factors for Fluopyram.** | |
|---|---|---|
| RAC | Processed Commodity | Average Processing Factor |
| Plum | Prune | 1.1 |
| | Washed fruit | 0.5 |
| Potato | Chips | 0.3 |
| | Flakes | 1.0 |
| | Wet peel | 4.3 |
| | Washed tubers | 0.7 |
| | Peeled tubers | 0.2 |
| | Cooked tubers | 0.2 |
| Soybean | Aspirated grain fractions | 222 |
| | Meal | 0.05 |
| | Refined oil | 0.02 |
| | Hulls | 1.3 |
| | Flour | 0.04 |
| | Soymilk | 0.01 |
| Strawberry | Washed and cooked (foliar treatment) | 0.9 |
| | Washing and cooking did not reduce the residue of fluopyram on strawberries treated by drip irrigation application | |
| Sugar beet | Dried pulp | 1.3 |
| | Refined sugar | 1.3 |
| | Molasses | 0.9 |
| Summer squash | Washed (foliar treatment) | 0.57 |
| | Washed and cooked (foliar treatment) | 0.46 |
| | Washed and cooked (drip irrigation) | 0.97 |
| Wheat | Aspirated grain fractions | 69.7 |
| | Flour | 0.1 |
| | Middlings | 0.3 |
| | Shorts | 0.8 |
| | Bran | 2.7 |
| | Germ | 2.4 |

[1] NC = not calculated. A processing factor could not be calculated because residues were below the LOQ in both the RAC and the processed commodity.

The available processing data indicate that tolerances are needed for fluopyram residues in apple wet pomace and processed potato waste (wet peel). The tolerances proposed by the petitioner for these commodities are too high; reduced tolerances of 0.60 ppm for apple wet pomace, 0.08 ppm for processed potato waste, are supported by the processing data. Although the available processing data indicate that fluopyram residues concentrate (1.3x or less) in prune, sugar beet dried pulp, sugar beet refined sugar, no tolerances are needed for these commodities as residues are not expected at levels exceeding the recommended RAC tolerance.

Apple

An apple processing trial was conducted to measure the magnitude of fluopyram residues in apples and apple processed commodities following exaggerated rate treatment. At one site in NY, two airblast applications of the 4.16 lb/gal SC formulation were made to apple trees at a rate of 1.125 lb ai/A and 1.115 lb ai/A, respectively, for a total amount applied of 2.24 lb ai/A (2511 g ai/ha), which is 5x the proposed maximum seasonal rate. The applications were made at spray volumes of 65 GPA (610 L/ha). The first application was made to the apples at the beginning of ripening (BBCH 81), with a 6-day interval between the two applications. Samples of apple fruit were collected 5 days following the last application and processed into apple wet pomace, juice, washed fruit, peeled fruit, applesauce, and dried fruit.

The apple samples and processed commodities were analyzed for residues of fluopyram using an adequate HPLC/MS/MS method, Method No. GM-001-P07-01. The LOQ was 0.01 ppm in each matrix. Sample storage conditions and durations are reported in Table 7; samples of fresh fruit and the processed commodities were stored frozen for up to ~9 months prior to analysis. The available storage stability data support the apple processing study.

The average fluopyram residues in/on apple RAC were 0.93 ppm. The average fluopyram residues for the required processed commodities were 2.14 ppm in apple wet pomace and 0.41 ppm in apple juice, and the average residues for the additional risk assessment samples were 0.65 ppm in washed fruit, 0.03 ppm in peeled fruit, 0.01 ppm in applesauce, and 0.03 ppm in dried fruit. Fluopyram residues were found to concentrate in apple wet pomace (2.3x processing factor) but did not concentrate in apple juice (0.4x), washed fruit (0.7x), peeled fruit (0.03x), applesauce (0.01x), or dried fruit (0.03x).

The processing factor for apple pomace is lower than the theoretical concentration factor of 14x for apple pomace (OPPTS 860.1520, Table 4).

*Conclusions*. The submitted processing data are adequate to satisfy data.

The processing data indicate that fluopyram residues concentrate in apple wet pomace. Based on the HAFT residues for fluopyram residues in/on apple from the North American field trials (0.255 ppm), and the processing factor from the North American processing study (2.3x), expected fluopyram residues in wet pomace would be 0.59 ppm. Therefore, a tolerance of 0.60 ppm would be appropriate for residues of fluopyram in wet apple pomace.

<u>Canola (proposed label revised as rotated)</u>

A canola processing trial was conducted to measure the magnitude of fluopyram residues in canola and canola processed commodities following exaggerated rate treatment. At one site in MN, two broadcast foliar spray applications of the 4.16 lb/gal SC formulation were made to canola plants at a rate of 1.166 lb ai/A and 1.116 lb ai/A, respectively, for a total amount applied of 2.28 lb ai/A (2.58 kg ai/ha). The applications were made at spray volumes of 17 GPA (161 L/ha) and 19 GPA (180 L/ha), respectively. The first application was made when 50% of pods ripe and thirteen days later the second application was made when 60% of pods ripe. Samples of canola were collected 14 days following the last application and processed into canola meal and oil.

The resultant canola samples and processed commodities were analyzed for residues of fluopyram using an adequate HPLC/MS/MS method, Method No. GM-001-P07-01. The LOQ was 0.01 ppm in each matrix. Sample storage conditions and durations are reported in Table 7; samples of canola seed and the canola processed commodities were stored frozen for up to ~12 months prior to analysis. The available storage stability data support the canola processing study.

The average fluopyram residues in/on canola seed were 0.83 ppm. The average fluopyram residues for the processed commodities were 0.28 ppm in canola meal and 0.01 ppm in canola oil. Fluopyram residues did not concentrate in canola meal (0.3x) or canola refined oil (refined, bleached and deodorized; 0.01x).

The processing factors for canola meal and canola oil are lower than the theoretical concentration factors of 1.9x for canola meal and 3.0x for canola oil (OPPTS 860.1520, Table 3).

*Conclusions*. The submitted processing data are adequate for estimating residue levels in potential livestock feedstuffs and for dietary exposure analysis.

Corn (proposed label revised as rotated)

A field corn processing trial was conducted to measure the magnitude of fluopyram residues in field corn, aspirated corn grain fractions, and corn processed commodities following exaggerated rate treatment. At one site in IL, two broadcast foliar applications of the 4.16 lb/gal SC formulation were made to field corn at a rate of 1.09 lb ai/A and 1.10 lb ai/A, respectively, for a total amount applied of 2.19 lb ai/A (2460 g ai/ha). The applications were made at spray volumes of 18 GPA (167-170 L/ha). Both applications were made at growth stage 87 (physiological maturity) with the second application occurring 7 days after the first. Samples of corn grain were collected 12 days after the last application and processed into AGF, starch, and refined/bleached/deodorized oil from wet milling, and grits, flour, meal, bran, and refined/bleached/deodorized oil from dry milling.

The resultant corn RAC samples and processed commodities were analyzed for residues of fluopyram using an adequate HPLC/MS/MS method, Method No. GM-001-P07-01. The LOQ was 0.01 ppm in field corn grain and all processed commodities except AGF. The LOQ was 2.00 ppm in AGF.

Sample storage conditions and durations are reported in Table 7; samples of field corn grain (RAC), AGF, and the corn processed commodities analyzed in this study were held in frozen storage for a maximum of ~13 months, 15 months, and 2 months, respectively, prior to analysis. The available storage stability data support the field corn processing study.

The average fluopyram residues in/on field corn grain were 0.028 ppm. The average fluopyram residues in/on field corn AGF were 4.48 ppm. The average fluopyram residues for the required processed commodities were <LOQ in field corn wet milled starch, 0.017 ppm in refined/bleached/deodorized oil (wet milled), 0.014 ppm in field corn grits, 0.024 ppm in field corn flour, 0.023 ppm in field corn meal, 0.074 ppm in field corn bran, and <LOQ in refined/bleached/deodorized oil (dry milled).

Fluopyram residues did not concentrate in field corn starch (0.2x), refined/bleached/deodorized oil (wet milled; 0.6x), field corn grits (0.5x), field corn flour (0.9x), field corn meal (0.8x), and refined/bleached/deodorized oil (dry milled; 0.1x). However, the residue did concentrate in field corn AGF (161x), and field corn bran (2.6x).

The processing factors determined for fluopyram residues in this study are less than the maximum theoretical concentration factor of 25x for corn oil (based on separation into components; OPPTS 860.1520, Table 3).

*Conclusions*. The submitted processing data are are adequate for estimating residue levels in potential livestock feedstuffs and for dietary exposure analysis.

Cotton (Rotated)

A cotton processing trial was conducted to measure the magnitude of fluopyram residues in cotton undelinted seed and cottonseed processed commodities following exaggerated rate treatment. At one site in AR, two broadcast applications of the 4.16 lb/gal SC formulation were made to bare ground at a rate of 1.11 lb ai/A and 1.12 lb ai/A, for a total amount applied of 2.23 lb ai/A (2500 g ai/ha), which is 5x the proposed maximum seasonal rate. Each application was made at a spray volume of 10 GPA (93-94 L/ha). Cotton was planted with a PBI of 12 days. Samples of seed cotton were harvested at the normal growth stage for commercial harvest and processed into cottonseed meal, hulls, and refined oil (bleached and deodorized).

The resultant cotton seed samples and processed commodities were analyzed for residues of fluopyram using an adequate HPLC/MS/MS method, Method No. GM-001-P07-01. The LOQ was 0.01 ppm in each matrix. Sample storage conditions and durations are reported in Table 7; samples of cottonseed and cottonseed processed commodities were stored frozen for up to ~7 months and <1 month, respectively, prior to analysis. The available storage stability data for rape seed are adequate and may be translated to support the cottonseed processing study. Storage stability data are not needed for cotton processed fractions since processed samples were stored less than 30 days.

The fluopyram residues in/on cottonseed and the processed commodities were less than the LOQ of 0.01 ppm following a 5x exaggerated rate of application of fluopyram. Therefore, processing factors could not be determined.

The maximum theoretical concentration factors based on separation into components are 3.8x for cotton hulls, 2.2x for cotton meal, and 6.3x for cotton oil (OPPTS 860.1520, Table 3).

*Conclusions*. The submitted cotton processing data are adequate to satisfy data requirements. No tolerances for cotton processed commodities are needed.

Melon

EPA does not require residue data for any processed commodities of muskmelons. However, the petitioner collected additional muskmelon samples in the North American field trials to determine possible residue reduction from peeling muskmelons.

From the muskmelon decline trial plot receiving two foliar broadcast or drip line irrigation applications, residue reduction subsamples of muskmelons, collected at 0- or 7-day PHI, were processed by peeling, and these subsamples were evaluated for residues of fluopyram.

The samples of muskmelon before and after peeling were analyzed for residues of fluopyram using an adequate HPLC/MS/MS method, Method No. GM-001-P07-01. The LOQ was 0.01

ppm in muskmelons. Sample storage conditions and durations are reported in Table 7; samples of muskmelon were stored frozen for up to ~7 months prior to analysis. The available storage stability data for lettuce are adequate to support the muskmelon processing study.

The average fluopyram residue found in/on unpeeled muskmelons (RAC) treated by broadcast foliar application was 0.151 ppm. The average fluopyram residue found in peeled muskmelons treated by broadcast foliar application was 0.0067 ppm. The calculated processing factor was 0.044x for peeling.

The average fluopyram residue found in/on unpeeled muskmelon (RAC) treated by drip line irrigation application was 0.0038 ppm. The average fluopyram residue found in peeled muskmelons treated by drip line irrigation application was 0.0027 ppm. The calculated processing factor was 0.71x for peeling.

*Conclusions*. The submitted processing data are not needed to satisfy data requirements; however the data may be used for risk assessment purposes.

<u>Peanut</u>

A peanut processing trial was conducted to measure the magnitude of fluopyram residues in peanut and peanut processed commodities following exaggerated rate treatment. At one site in GA, two broadcast foliar spray applications of the 4.16 lb/gal SC formulation were made to peanuts at a rate of 1.116 lb ai/A and 1.117 lb ai/A, respectively, for a total amount applied of 2.233 lb ai/A (2500 g ai/ha), which is 5x the proposed maximum seasonal rate. The first application was made at growth stage of BBCH 88 (about 80% of pods developed to final size are ripe) with the second application occurring 13 days later at growth stage of BBCH 89 (nearly all pods developed to final size are ripe). Each application was made at a spray volume of 15 GPA (138 to 144 L/ha). Samples of peanuts were collected 6 days following the last application and processed into peanut meal, refined oil, dry roasted peanut, and peanut butter.

The resultant peanut nutmeat (RAC) sample and processed commodities were analyzed for residues of fluopyram using an adequate HPLC/MS/MS method, Method No. GM-001-P07-01. The LOQ was 0.01 ppm in each matrix. Sample storage conditions and durations are reported in Table 7; samples of peanut nutmeat and the peanut processed commodities were stored frozen for up to ~12 months prior to analysis. The available storage stability data support the peanut processing study.

The average fluopyram residues in/on peanut nutmeat (RAC) were 0.094 ppm. The average fluopyram residues for the required processed commodities were 0.018 ppm in meal and 0.023 ppm in refined oil, and the average residues for the additional risk assessment samples were 0.024 ppm in dry roasted peanuts and 0.021 ppm in peanut butter. Fluopyram residues did not concentrate in the processed commodities of meal (0.2x processing factor), refined oil (0.2x), dry roasted peanuts (processing factor = 0.3x), and peanut butter (0.2x).

The processing factors determined for fluopyram residues in this study are less than the theoretical processing factors of 2.2x for peanut meal and 2.8x for peanut oil (based on separation into components; OPPTS 860.1520, Table 3).

*Conclusions*. The submitted peanut processing data are adequate to satisfy data requirements. The data indicate that no tolerances are needed for peanut processed commodities.

Plum

A plum processing trial was conducted to measure the magnitude of fluopyram residues in plums and plum processed commodities following exaggerated rate treatment. At one site in CA, two airblast applications of the 4.16 lb/gal SC formulation were made to plum trees at a rate of 1.116 lb ai/A and 1.117 lb ai/A, respectively, for a total amount applied of 2.23 lb ai/A (2503 g ai/ha) which is >5x the proposed maximum seasonal rate. The applications were made at spray volumes of 50 GPA (469-470 L/ha). The first application was made to the plums at fruit ripe for picking (BBCH 87), with a 7-day interval between the two applications. Samples of plum fruit were collected on the day of the last application and processed into prunes and washed fruit.

The resultant plum samples and processed commodities were analyzed for residues of fluopyram using an adequate HPLC/MS/MS method, Method No. GM-001-P07-01. The LOQ was 0.01 ppm in each matrix. Sample storage conditions and durations are reported in Table 7; samples of plum fresh fruit and the plum processed commodities were stored frozen for ~10 months prior to analysis. The available storage stability data support the plum processing study.

The average fluopyram residues in/on plum (RAC) were 0.18 ppm. The average fluopyram residues for the required processed commodity were 0.21 ppm in/on prune. The average fluopyram residue data for additional risk assessment samples were 0.09 ppm in/on washed fruit. The fluopyram residue was found to concentrate in prunes (1.1x). No concentration (<1x) of fluopyram residue was found in washed fruit (0.5x).

The processing factors determined for fluopyram residue in this study are less than the maximum theoretical concentration factor (based on loss of water) of 3.4x for prunes (OPPTS 860.1520, Table 2).

*Conclusions*. The submitted plum processing data are adequate to satisfy data requirements.

The data indicate that fluopyram residues concentrate in prunes. Using the HAFT of 0.283 ppm and the 1.1x processing factor, the expected residues in prunes following treatment at 1x would be 0.31 ppm, which is less than the recommended tolerance of 0.35 ppm for plum. No tolerance is needed for prunes.

Potato

A potato processing trial was conducted to measure the magnitude of fluopyram residues in potato and potato processed commodities following exaggerated rate treatment. At one site in MN, two broadcast foliar spray applications of the 4.16 lb/gal SC formulation were made to potatoes at a rate of 1.123 lb ai/A and 1.124 lb ai/A, respectively, for a total amount applied of 2.25 lb ai/A (2545 g ai/ha) which is >5x the proposed maximum seasonal rate. The applications were made at spray volumes of 17 GPA (161 L/ha). The first application was made at the end of flowering in the first inflorescence (BBCH 69) and the second application, 4 days later, berries in the fructification ochre-colored (BBCH 85). Samples of potato were collected 6 days following the last application and processed into the required processed commodities of wet peel, potato chips, and potato flakes. In addition, samples of washed potatoes, tuber without peel, and cooked potatoes were generated for use in the dietary risk assessment for fluopyram.

The resultant potato samples and processed commodities were analyzed for residues of fluopyram using an adequate HPLC/MS/MS method, Method No. GM-001-P07-01. The LOQ was 0.01 ppm in each matrix. Sample storage conditions and durations are reported in Table 7; samples of potato tuber and the potato processed commodities were stored frozen for ~10 months prior to analysis. The available storage stability data support the potato processing study.

The average fluopyram residues in/on potato tubers (RAC) were 0.016 ppm. The average fluopyram residues for the required processed commodities were 0.069 ppm in potato wet peel, <0.01 ppm in potato chips and 0.02 ppm in potato flakes. The average fluopyram residue data for additional risk assessment samples were 0.01 ppm in washed tubers, and <0.01 ppm in both peeled and cooked tubers. The fluopyram residue did not concentrate in the required processed commodities of potato chips (0.3x processing factor) and potato flakes (1x). However, the residue did concentrate in potato wet peel (4.3x). In the additional samples generated for dietary risk assessment, fluopyram residue did not concentrate in washed tubers (0.7x), and peeled and cooked tubers (0.2x).

The processing factors determined for fluopyram residues in this study are less than the maximum theoretical concentration (processing) factor of 5.0x for potatoes (OPPTS 860.1520, Table 1).

*Conclusions*. The submitted potato processing data are adequate to satisfy data requirements.

The processing data indicate that fluopyram residues concentrate in wet peel. Using the HAFT of 0.017 ppm and the 4.3x processing factor, the expected residues in potato wet peel following treatment at 1x would be 0.073 ppm. These data support a tolerance of 0.08 ppm for processed potato waste.

<u>Soybean (proposed label revised as rotated)</u>

A soybean processing trial was conducted to measure the magnitude of fluopyram residues in soybean seed, AGF, and soybean processed commodities following exaggerated rate treatment. At one site in KS, two broadcast foliar applications of the 4.16 lb/gal SC formulation were made to soybean at a rate of 1.11 lb ai/A/application (1250 g ai/ha/application), for a total amount applied of 2.23 lb ai/A (2500 g ai/ha). The first application was made at growth stage BBCH 79 (all pods reached final length) with the second application occurring 7 days later at growth stage BBCH 81 (10% pods ripe, beans final color, dry and hard). Each application was made at a spray volume of 15 GPA (138 L/ha). Samples of soybean seed were collected 13 days after the last application and processed into AGF, and the required processed commodities of meal, hulls, and oil (refined, bleached and deodorized). In addition, defatted flour and soymilk were generated for risk assessment purposes.

The resultant soybean RAC samples and processed commodities were analyzed for residues of fluopyram using an adequate HPLC/MS/MS method, Method No. GM-001-P07-01. The LOQ was 0.01 ppm in soybean seed and all processed commodities except AGF. The LOQ was 0.10 ppm in AGF. Sample storage conditions and durations are reported in Table 7; samples of soybean seed (RAC), AGF, and the soybean processed commodities analyzed in this study were held in frozen storage for a maximum of ~12 months, ~13 months, and ~2 months, respectively, prior to analysis. The available storage stability data support the soybean processing study.

The average fluopyram residues in/on soybean seed were 0.49 ppm. The average fluopyram residues in/on soybean AGF were 110 ppm. The average fluopyram residues for the required processed commodities were 0.02 ppm in soybean meal, 0.64 ppm in soybean hulls, and 0.01 ppm in soybean refined oil. The average fluopyram residue data for additional risk assessment samples were 0.02 ppm in soybean flour and <0.01 ppm in soybean milk. Fluopyram residues did not concentrate (processing factor <1x) in the processed commodities of soybean meal (0.05x), soybean refined oil (0.02x), soybean flour (0.04x) or soybean soymilk (0.01x). However, the residue did concentrate in soybean hulls (1.3x) and in soybean AGF (222x).

The processing factors determined for fluopyram residue in this study are less than the maximum theoretical concentration factors based on separation into components of 11.3x for soybean hulls, 2.2x for soybean meal, and 12.0x for soybean oil (OPPTS 860.1520, Table 3).

*Conclusions*. The submitted soybean processing data are adequate for estimating residue levels in potential livestock feedstuffs and for dietary exposure analysis.

Strawberry

EPA does not require residue data for any processed commodities of strawberry. However, the petitioner collected additional strawberry samples in the field trials to determine possible residue reduction from washing strawberries and from cooking strawberries.

From the decline trial plot receiving two foliar broadcast applications, subsamples of strawberries, collected at a 0-day PHI, were processed by washing and by washing and cooking, and these subsamples were evaluated for residues of fluopyram. From the decline trial plot receiving two drip irrigation applications, subsamples of strawberries, collected at a 7-day PHI, were processed by washing and cooking, and these subsamples were evaluated for residues of fluopyram. The washing and cooking procedures were performed in a manner similar to normal household practice.

The washed and cooked strawberry samples were analyzed for residues of the parent compound, fluopyram using an adequate HPLC/MS/MS method, Method No. GM-001-P07-01. The LOQ was 0.01 ppm in each matrix. Sample storage conditions and durations are reported in Table 7; samples of strawberries and strawberry processed commodities were stored frozen for up to ~7 months prior to analysis. The available storage stability data support the strawberry processing study.

The average fluopyram residues in/on strawberries treated by foliar broadcast application were reduced from an average of 0.445 ppm in/on the RAC to an average of 0.327 ppm in washed fruit and 0.328 ppm in washed and cooked fruit. The average fluopyram residues in/on strawberries treated by drip line irrigation application were the same in/on the strawberry RAC (0.014 ppm) as in the washed and cooked strawberries (0.014 ppm). The average processing factor for washed and cooked fruit was 0.9x.

*Conclusions*. The submitted processing data are not needed to satisfy data requirements; however the data may be used for risk assessment purposes.

Summer squash

EPA does not require residue data for any processed commodities of summer squash. However, the petitioner collected additional summer squash samples in the North American field trials to determine possible residue reduction from washing or cooking summer squash.

From the summer squash decline trial plot receiving two foliar broadcast or drip line irrigation applications, residue reduction subsamples of summer squash, collected at 0- or 7-day PHI, were processed by washing or cooking, and these subsamples were evaluated for residues of fluopyram.

The samples of summer squash before and after washing or cooking were analyzed for residues of fluopyram using an adequate HPLC/MS/MS method, Method No. GM-001-P07-01. The LOQ was 0.01 ppm in summer squash. Sample storage conditions and durations are reported in Table 7; samples of summer squash were stored frozen for up to ~9 months prior to analysis. The available storage stability data for lettuce are adequate to support the summer squash processing study.

The average fluopyram residue found in/on summer squash (RAC) treated by broadcast foliar application was 0.0684 ppm. The average fluopyram residue found in washed and cooked summer squash treated by broadcast foliar application were 0.0388ppm and 0.0317 ppm, respectively. The calculated processing factors were 0.57x for washing and 0.46x for cooking.

The average fluopyram residue found in/on summer squash (RAC) treated by drip line irrigation application was 0.0112 ppm. The average fluopyram residue found in washed and cooked summer squash treated by drip line irrigation application was 0.011 ppm. The calculated processing factor was 0.97x for cooking.

*Conclusions*. The submitted processing data are not needed to satisfy data requirements; however the data may be used for risk assessment purposes.

Sugar beet

A sugar beet processing trial was conducted to measure the magnitude of fluopyram residues in sugar beet roots and sugar beet processed commodities following exaggerated rate treatment. At one site in MN, two broadcast foliar spray applications of the 4.16 lb/gal SC formulation were made to sugar beet plants at a rate of 1.155 lb ai/A and 1.048 lb ai/A, respectively, for a total amount applied of 2.20 lb ai/A (2494 g ai/ha), which is >5x the proposed maximum seasonal rate. The applications were made at spray volumes of 18 GPA (170 L/ha) and 17 GPA (161 L/ha), respectively. The first application was made when the beet-root had reached harvestable size (BBCH 49) and the second application 6 days later (BBCH 49). A single composite sample of sugar beet roots was dug at a 7-day PHI (BBCH 49) and processed into sugar beet dried pulp, molasses, and refined sugar.

The resultant sugar beet root samples and processed commodities were analyzed for residues of fluopyram using an adequate HPLC/MS/MS method, Method No. GM-001-P07-01. The LOQ was 0.01 ppm in each matrix. Sample storage conditions and durations are reported in Table 7; samples of sugar beet root and the sugar beet processed commodities were stored frozen for ~13 months and ~3 months, respectively, prior to analysis. The available storage stability data support the sugar beet processing study.

The average fluopyram residues in/on sugar beet root (RAC) were 0.26 ppm. The average fluopyram residues for the processed commodities were 0.33 ppm in dried pulp, 0.33 ppm in refined sugar, and 0.25 ppm in molasses. The fluopyram residue did not concentrate in the processed commodity of molasses (0.9x processing factor). However, the residue did concentrate slightly in dried pulp and refined sugar (1.3x).

The processing factors determined for fluopyram residue in this study are less than the maximum observed (theoretical) concentration factor of 20x for sugar beet dry pulp and the theoretical concentration factor (based on separation into components) of 12.5x for sugar (OPPTS 860.1520, Tables 3 and 4).

*Conclusions*. The submitted sugar beet processing data are adequate to satisfy data requirements.

The processing data indicate that fluopyram residues concentrate in sugar beet dried pulp and refined sugar. Using the HAFT of 0.02 ppm and the 1.3x processing factor, the expected residues in dried pulp and refined sugar following treatment at 1x would be <0.03 ppm. Because these values are less than the recommended tolerance of 0.04 ppm for sugar beet root, no tolerances are needed for sugar beet dried pulp or refined sugar.

<u>Wheat (proposed label revised as rotated)</u>

A wheat processing trial was conducted to measure the magnitude of fluopyram residues in wheat grain, aspirated wheat grain fractions, and wheat processed commodities following exaggerated rate treatment. At one site in MN, two broadcast foliar spray applications of the 4.16 lb/gal SC formulation were made to wheat at a rate of 1.16 lb ai/A and 1.17 lb ai/A, respectively, for a total amount applied of 2.33 lb ai/A (2610 g ai/ha). Each application was made at a spray volume of 18 GPA (164-167 L/ha). The first application was made at growth stage of BBCH 77 (late milk) with the second application occurring 13 days later at growth stage of BBCH 89 (fully ripe). Samples of wheat grain were collected 14 days after the last application and processed into AGF and the required processed commodities of bran, flour, shorts, middlings, and germ.

The resultant wheat samples and processed commodities were analyzed for residues of fluopyram using an adequate HPLC/MS/MS method, Method No. GM-001-P07-01. The LOQ was 0.01 ppm in wheat grain, 0.10 ppm in wheat bran, flour, middlings, shorts, and germ, and 0.20 ppm in AGF. Sample storage conditions and durations are reported in Table 7; samples of wheat grain (RAC), AGF, and the wheat processed commodities analyzed in this study were held in frozen storage for a maximum of ~11 months, ~11 months, and <1 month, respectively, prior to analysis. The available storage stability data for wheat grain support wheat grain and aspirated grain sample storage durations and conditions. Storage stability data are not needed for wheat processed fractions since processed samples were stored less than 30 days.

The average fluopyram residues in/on wheat grain were 1.57 ppm. The average fluopyram residues in/on wheat AGF were 109 ppm. The average fluopyram residues for the required processed commodities were 4.23 ppm in wheat bran, 0.19 ppm in wheat flour, 3.80 ppm in wheat germ, 0.53 ppm in wheat middlings, and 1.18 ppm in wheat shorts. Fluopyram residues did not concentrate (processing factor <1x) in the processed commodities of wheat flour (0.1x), wheat middlings (0.3x), and wheat shorts (0.8x). However, the residue did concentrate in wheat AGF (69.7x), wheat bran (2.7x), and wheat germ (2.4x).

The processing factors determined for fluopyram residue in this study are less than the maximum theoretical concentration factors of 7.7x for wheat bran, 1.4x for wheat flour, and 8.3x for wheat shorts (OPPTS 860.1520, Table 3; based on separation into components).

*Conclusions*. The submitted wheat processing data are adequate for estimating residue levels in potential livestock feedstuffs and for dietary exposure analysis.

**860.1650 Submittal of Analytical Reference Standards**

Analytical standard for fluopyram is currently available in the EPA National Pesticide Standards Repository (personal communication with Charles Stafford, ACB, 6/14/11). However, no standard is available for AE C656948-benzamide. The registrant is required to submit a reasonable amount of the analytical reference standard for the benzamide. The reference standard should be sent to the Analytical Chemistry Lab, which is located at Fort Meade, Maryland, to the attention of either Theresa Cole or Thuy Nguyen at the following address:

USEPA
National Pesticide Standards Repository/Analytical Chemistry Branch/OPP
701 Mapes Road
Fort George G. Meade, MD 20755-5350

(Note that the mail will be returned if the extended zip code is not used.)

**860.1850 Confined Accumulation in Rotational Crops**

First Entry Monograph for Fluopyram, Section B.7.9.1 (MRIDs 47372631 and 47372632)

Bayer submitted confined rotational crops studies with fluopyram labeled in the phenyl and the pyridyl rings.

MRID 47372631: The metabolism of the fungicide fluopyram was investigated in the rotational crops wheat, Swiss chard, and turnips from three consecutive rotations. [phenyl-UL-$^{14}C$]Fluopyram was applied uniformly onto to bare soil in a planting container (area approx. 1 $m^2$) by spray application. The application rate amounted to 534 g ai/ha (0.476 lb ai/A) which is ~1.1x the proposed maximum seasonal rate. Crops of the 1st, 2nd and 3rd rotation were sown 30 days, 139 days, and 280 days after soil application. See Table 27 below for summary results.

**Table 27. Total Radioactive Residues (TRRs) in crops at different PBI**

| TRR (ppm) | Wheat | | | | Swiss chard | Turnip | |
|---|---|---|---|---|---|---|---|
| | Forage | Hay | Straw | Grain | | Tops | Root |
| First rotation (30 days) | 0.100 | 1.783 | 6.156 | 0.167 | 0.540 | 0.884 | 0.065 |
| Second rotation (139 days) | 0.785 | 1.120 | 3.450 | 0.054 | 0.377 | 0.113 | 0.013 |
| Third rotation (280 days) | 0.197 | 1.527 | 1.032 | 0.023 | 0.164 | 0.103 | 0.009 |

TRR accumulated at ≥0.01 ppm in all rotated crop matrices from all PBIs, except turnip roots from the 280-day PBI. TRR ranged from 0.009 ppm in turnip roots planted 280 days after soil application to 6.156 ppm in mature wheat straw planted 30 days after soil application. TRR generally declined with the later PBIs, except in wheat forage in which residues increased at the 139-day PBI, but decreased at the 280-day PBI, to approximately 2x the initial value.

Conventional extraction of the RACs using ACN/water released >96% of the radioactive residues in Swiss chard and turnip leaves and roots, 87-95% of the radioactive residues in wheat forage, hay, and straw, and 77-85% of the radioactive residues in wheat grain. Turnip roots from the 280-day PBI were not subjected to extraction procedures due to low TRR. The post extraction solids of wheat hay (all rotations) and wheat straw (1st and 2nd rotation) were exhaustively extracted using ACN/water in a microwave with increased temperature. Microwave extraction released a further 3-5% TRR in wheat hay and straw. Conventional and microwave extracts of wheat hay and straw showed similar metabolite patterns. Diastase treatment of the post extraction solids of wheat grain released a further 9% TRR from the solids of the 1st rotation, and 15% TRR from the solids of the 2nd rotation. The solutions after diastase treatment were further characterized as polar and probably natural compounds by partitioning (1st rotation). Nonextractable residues remaining after all extractions were <10% TRR in all rotated crop RACs from all PBIs, except 280-day PBI wheat grain in which the nonextractable residues were 21.9% TRR, but represented 0.005 ppm.

Parent fluopyram and 28 metabolites were detected in the various samples of the three rotations. Of these, the active substance and 12 metabolites were identified by HPLC/MS and HPLC/MS/MS. The other 16 metabolites (unknowns) were characterized by their extraction and retention in radio-HPLC; each of them were <0.04 ppm. Additionally, a very polar region was characterized in wheat grain, accounting for up to 21.3% TRR (0.01 ppm) in the second rotation, which the petitioner concluded could be due to assimilated $^{14}CO_2$ which was incorporated in the starch matrix.

Parent fluopyram accounted for the major part of the residues in all RACs of all rotations, at 56-84% TRR in the RACs of the 1st rotation, 33-78% TRR in the RACs of the 2nd rotation, and 28-59% TRR in the RACs in the 3rd rotation. Fluopyram was found at levels ≥0.01 ppm in all rotational crop commodities from the 30- and 139-day PBIs and in all commodities except wheat grain and turnip root from the 280-day PBI. In general, the levels of the parent compound decreased with subsequent PBIs. AE C656948-7-hydroxy and its various conjugates with glucose, malonic acid (2 isomers), and sulfuric acid were important metabolites mainly in Swiss chard, where AE C656948-7-hydroxy accounted for 21% TRR in the 1st rotation, increasing to about 35% TRR in the following rotations. In the other RACs, levels of AE C656948-7-hydroxy were lower, at <10% TRR, except in wheat hay and straw from the 3rd rotation in which AE C656948-7-hydroxy accounted for 12.3-12.6% TRR. The sulfuric acid conjugate of AE C656948-7-hydroxy, AE C656948-7-OH-SA, was also a prominent metabolite in Swiss chard, increasing from 7% TRR in the 1st rotation to 16% and 12% TRR in the 2nd and 3rd rotations, respectively. AE C656948-7-OH-SA was also detected at low levels in turnip leaves (0.7-1.0% TRR; 30- and 139-day PBIs), but not in the other rotated crop RACs.

Two label-specific metabolites were identified: AE C656948-benzamide and AE C656948-benzoic acid. AE C656948-benzoic acid accounted for 0.6-6.9% TRR in wheat forage, hay, and grain, and turnip leaves and roots from the 30-day PBI; 0.3-0.4% TRR in wheat forage and hay, and 13.6% TRR in wheat grain from the 139-day PBI; and 13% TRR in wheat grain from the

280-day PBI. AE C656948-benzamide accounted for 2.8-9.7% TRR in wheat forage, hay, straw, and grain, and turnip leaves and roots, and 11.1% TRR in Swiss chard from the 30-day PBI; 3.2-7.4% TRR in all RACs from the 139-day PBI; and 5.9-8.0% TRR in wheat forage, hay, straw, and grain, and 10.3-11.7% TRR in Swiss chard and turnip leaves from the 280-day PBI.

AE C656948-8-hydroxy and its conjugate were only of minor importance. Both or at least one of them were detected in all RACs but at very low levels (<2.7% TRR in total). AE C656948-phenol-glc was detected in turnip leaves only, where it amounted to 10%, 16%, and 10% TRR in the 1st, 2nd, and 3rd rotations, respectively.

MRID 47372632: The metabolism of the fluopyram was investigated in the rotational crops wheat, Swiss chard, and turnips from three consecutive rotations. [pyridyl-2,6-$^{14}$C]Fluopyram was applied uniformly onto bare soil in a planting container (area approx. 1 $m^2$) by spray application. The application rate amounted to 514 g ai/ha (0.459 lb ai/A), which is 1x the proposed maximum seasonal rate. Crops of the 1st, 2$^{nd}$, and 3rd rotation were sown 30 days, 139 days and 280 days after soil application, respectively. See Table 28 below for summary results.

**Table 28. Total Radioactive Residues (TRRs) in crops at different PBI**

| TRR (ppm) | Wheat | | | | Swiss chard | Turnip | |
|---|---|---|---|---|---|---|---|
| | Forage | Hay | Straw | Grain | | Tops | Root |
| First rotation (30 days) | 0.157 | 1.802 | 6.663 | 0.412 | 0.570 | 0.565 | 0.036 |
| Second rotation (139 days) | 0.568 | 0.971 | 2.562 | 0.072 | 0.343 | 0.103 | 0.010 |
| Third rotation (280 days) | 0.167 | 0.709 | 1.622 | 0.037 | 0.211 | 0.095 | 0.012 |

TRR accumulated at ≥0.01 ppm in all rotated crop matrices from all PBIs. TRR ranged from 0.010 ppm in turnip roots planted 139 days after soil application to 6.663 ppm in mature wheat straw planted 30 days after soil application. TRR generally declined with the later PBIs, except in wheat forage in which residues increased at the 139-day PBI, but returned to the initial levels at the 280-day PBI.

Conventional extraction of the RACs using ACN/water released >97% of the radioactive residues in Swiss chard and turnip leaves and roots, 85-96% of the radioactive residues in wheat forage, hay, and straw, and 82-92% of the radioactive residues in wheat grain. The post extraction solids of wheat hay (2nd and 3rd rotation) and wheat straw (1st and 2nd rotation) were exhaustively extracted using ACN/water in a microwave with increased temperature. Microwave extraction released a further 3-6% TRR in wheat hay and straw. Conventional and microwave extracts of wheat hay and straw showed similar metabolite patterns. Diastase treatment of the post extraction solids of wheat grain released a further 4% TRR from solids of the 1st rotation, and 9% TRR from the solids of the 2nd rotation. The solutions after diastase treatment were further characterized as polar and probably natural compounds by partitioning (1st rotation only). Nonextractable residues remaining after all extractions were <10% TRR in all rotated crop RACs from all PBIs, except 280-day PBI wheat grain in which the nonextractable residues were 17.8% TRR, but represented 0.007 ppm.

Parent fluopyram and 29 metabolites were detected in the various rotated crop samples of the three rotations. Of these, the active substance and 12 metabolites were identified by HPLC/MS, HPLC/MS/MS, and co-chromatography. The other 17 metabolites (unknowns) were characterized by their extraction and retention in radio-HPLC; each were ≤0.011 ppm representing 0.1-2.0% TRR, except the unknown metabolites in wheat straw, each of which were in the range of 0.4-1.3% TRR and equivalent to 0.011-0.042 ppm.

Apart from wheat grain, the parent compound was the main compound in all RACs of all rotations and accounted for 57-86% TRR in the RACs of the 1st rotation, 37-95% TRR in the RACs of the 2nd rotation, and 39-92% TRR in the RACs of the 3rd rotation. Fluopyram was found at levels ≥0.01 ppm in all rotational crop commodities from all three PBIs. In wheat grain, the parent accounted for 20.4 - 33.4% TRR in the three rotations. AE C656948-7-hydroxy and its various conjugates with glucose, malonic acid (two isomers) and sulfuric acid were important metabolites mainly in Swiss chard, where the AE C656948-7-hydroxy accounted for 28% TRR in the 1st rotation increasing to 37-39% TRR in the following rotations. In the other RACs, the amount of AE C656948-7-hydroxy was lower (≤10% TRR). The sulfuric acid conjugate of AE C656948-7-hydroxy, AE C656948-7-OH-SA, was also a prominent metabolite in Swiss chard, increasing from 8% TRR in the 1st rotation to 17% and 14% TRR in the 2nd and 3rd rotations, respectively; AE C656948-7-OH-SA was also found at low levels (<1% TRR) in turnip leaves from all PBIs. AE C656948-7-hydroxy-glc, and AE C656948-7-hydroxy-glc-MA (isomers 1 and 2) were minor metabolites (<10% TRR) in wheat forage, hay, and straw, Swiss chard, and/or turnip leaves.

Two label-specific metabolites were identified: AE C656948-PCA and AE C656948-methyl-sulfoxide. They formed the major part of the residues in wheat grain (totaling 48.9 - 65.4% TRR in the three rotations); AE C656948-PCA amounted to 56%, 16% and 29% TRR in the 1st, 2nd and 3rd rotation, respectively, and AE C656948-methyl-sulfoxide amounted to 1.2%, 49% and 20% TRR in the 1st, 2nd and 3rd rotation, respectively. AE C656948-PCA and AE C656948-methyl sulfoxide were also detected in other rotated crop RACs. AE C656948-PCA accounted for 17% TRR in 30-day PBI wheat forage and <10% TRR in wheat forage from subsequent PBIs, as well as in wheat hay, wheat straw (found in 1st rotation only), Swiss chard, turnip leaves, and turnip roots (1st rotation only). AE C656948-methyl-sulfoxide was identified in wheat forage, hay, and straw, and Swiss chard at low levels (<5% TRR).

AE C656948-8-hydroxy and its conjugate were only of minor importance. Both or at least one of them were detected in all RACs but at very low levels (<2.9% TRR in total). AE C656948-phenol-glc was detected in turnip leaves only, where it amounted to 12%, 18% and 15% TRR in the 1st, 2nd and 3rd rotation, respectively.

*Conclusions*. The submitted studies are adequate to satisfy data requirements.

Based on the results of the studies, metabolism of fluopyram in rotated crops appears to occur via:

- hydroxylation of the ethylene linking group of the parent compound forming AE C656948-7-hydroxy and -8-hydroxy metabolites;
- hydroxylation of the phenyl ring and subsequent conjugation with glucose;
- conjugation of the hydroxylated metabolites with glucose, malonic acid, and sulfuric acid;
- hydrolytic cleavage and subsequent oxidation to AE C656948-benzamide, AE C656948-benzoic acid, AE C656948-pyridyl carboxylic acid, and AE C656948-methyl sulfoxide; and

- formation of polar, probably natural compounds which were incorporated into the starch matrix of grains.

The petitioner stated that AE C656948-pyridyl carboxylic acid and AE C656948-methyl sulfoxide were possibly formed at low proportions in the soil or by enzymes located in the roots of the plants, and selectively translocated into grains following phloem transport.

The proposed metabolic pathway is very similar to that for primary crops. In rotational Swiss chard and turnip leaves, a sulfate conjugate (AE C656948-7-OH-SA) was found which was not found in primary crops. In rotational turnip leaves, hydroxylation of the ethylene linkage and hydroxylation in the phenyl-ring and subsequent conjugation with glucose was observed, leading to AE C656948-phenol-glc which was not found in primary crops. The metabolites AE C656948-benzoic acid and conjugates of AE C656948-8-hydroxy were also found in rotational crops and not in primary crops.

The residue of concern in rotational crops for tolerance enforcement is fluopyram; the residue of concern in rotated crops except in legumes and oilseed crops for risk assessment is fluopyram, and in rotated legumes and oilseed crops is fluopyram plus C656948-benzamide (ROCKS decision memo, 7/16/2009). Based on the results of the confined rotational crop studies, field rotational crop studies are needed for fluopyram.

## 860.1900 Field Accumulation in Rotational Crops

Second Entry Monograph for Fluopyram, Section B.7.9.2 (MRIDs 47567123-47567125)

Bayer submitted field rotational crop data from three studies. Two extensive field rotational crop studies were conducted with alfalfa and cotton with a target PBI of 14 days. In addition, a limited rotational crop study was conducted with wheat, turnip, and mustard greens with a PBI of approximately 240 days. The results of the field rotational crop studies are summarized in Table 29 and discussed below.

**Table 29. Summary of Results of Field Rotational Studies.**

| Commodity | Total Application Rate (lb ai/A) [kg ai/ha] | PBI (days) | Fluopyram Residue Levels (ppm) | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | n | Min. | Max. | HAFT | Median | Mean | Std. Dev. |
| **ROTATED ALFALFA ((proposed use = 0.450 lb ai/A maximum seasonal rate to annual crops, 14-day PBI)** | | | | | | | | | |
| Alfalfa forage; 1st cutting | 0.444-0.459 (0.497-0.514) | 12-14 | 24 | <0.01 | 0.39 | 0.33 | 0.04 | 0.07 | 0.09 |
| Alfalfa forage; 2nd cutting | | | 22 | <0.01 | 0.10 | 0.1 | 0.04 | 0.05 | 0.03 |
| Alfalfa forage; 3rd cutting | | | 22 | 0.01 | 0.19 | 0.17 | 0.03 | 0.05 | 0.05 |
| Alfalfa hay; 1st cutting | 0.444-0.459 (0.497-0.514) | 12-14 | 24 | 0.02 | 0.93 | 0.93 | 0.09 | 0.21 | 0.28 |
| Alfalfa hay; 2nd cutting | | | 22 | 0.01 | 0.36 | 0.35 | 0.11 | 0.13 | 0.11 |
| Alfalfa hay; 3rd cutting | | | 22 | 0.01 | 0.46 | 0.42 | 0.06 | 0.13 | 0.13 |

| Table 29. Summary of Results of Field Rotational Studies. | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Commodity | Total Application Rate (lb ai/A) [kg ai/ha] | PBI (days) | Fluopyram Residue Levels (ppm) | | | | | | |
| | | | n | Min. | Max. | HAFT | Median | Mean | Std. Dev. |
| **ROTATED COTTON (proposed use = 0.450 lb ai/A maximum seasonal rate to annual crops, 14-day PBI)** | | | | | | | | | |
| Undelinted cottonseed | 0.442-0.456 (0.495-0.511) | 12-14 | 22 | <0.01 | <0.01 | <0.01 | 0.01 | 0.01 | NA |
| Cotton gin byproducts | | | 10 | <0.01 | 0.02 | 0.02 | 0.01 | 0.01 | 0.01 |
| **OTHER ROTATED CROPS (proposed use = 0.450 lb ai/A maximum seasonal rate to annual crops, other than alfalfa and cottonl)** | | | | | | | | | |
| Turnip roots | 0.440 - 0.456 (0.493 - 0.511) | 228-236 | 6 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | NA |
| Turnip tops | | | 6 | <0.01 | 0.0408 | 0.0344 | 0.0180 | 0.0189 | 0.0014 |
| Mustard greens | 0.440 – 0.445 (0.493 – 0.499) | 228-236 | 6 | <LOQ | 0.0363 | 0.0348 | 0.0131 | 0.0176 | 0.0138 |
| Wheat forage | 0.450 - 0.467 (0.505 - 0.525) | 236-248 | 6 | <0.01 | 0.0481 | 0.0412 | 0.0104 | 0.0195 | 0.0174 |
| Wheat hay | | | 6 | 0.0177 | 0.0892 | 0.0819 | 0.0322 | 0.0442 | 0.0302 |
| Wheat grain | | | 6 | <0.01 | <0.01 | <0.01 | <0.01 | <0.01 | NA |
| Wheat straw | | | 6 | 0.0112 | 0.124 | 0.124 | 0.0314 | 0.0558 | 0.0536 |

Alfalfa (MRID 47567124): A total of 12 field trials were conducted during the 2007 growing season to measure the magnitude of fluopyram residues in alfalfa forage and hay planted as a rotational crop following crops treated with fluopyram. Trials were conducted in Zone 1 (PA), 2 (GA), 5 (IA, OH, NE, IN, ND, MN), 7 (ND), 9 (ID), 10 (CA), and 11 (ID). Two foliar spray applications of the 4.16 lb/gal SC formulation (AE C656948 500 SC) were made to a cover crop or bare soil at a target rate of 0.223 lb ai/A/application (0.215 to 0.232 lb ai/A/application) for a total target application rate of 0.446 lb ai/A (0.444 to 0.459 lb ai/A or 0.497 to 0.514 kg ai/ha; 1x the proposed maximum seasonal rate to annual crops). The interval between applications was 5-6 days. Alfalfa was planted at a target PBI of 14 days at each site; the actual PBI ranged from 12 to 14 days. All applications were made using ground-based equipment.

At each trial, duplicate treated samples of rotated alfalfa forage and hay were collected at each cutting. A single composite control sample of alfalfa forage and hay was also taken from an untreated plot at the time of the first cutting. Hay was allowed to air dry in the field at each cutting. In eleven of the field trials, three cuttings were performed; in one trial, alfalfa forage and hay were only collected from a single cutting.

The alfalfa forage and hay samples were analyzed for residues of the parent compound using an adequate HPLC/MS/MS method, Method No. GM-001-P07-01. The LOQ was 0.01 ppm in alfalfa forage and hay. Sample storage conditions and durations are reported in Table 7; samples were stored frozen for up to ~11 months prior to analysis. The available storage stability data support the field rotational crop study.

The results of the field rotational crop studies are summarized in Table 29. Quantifiable residues of fluopyram were found in/on alfalfa forage and hay from all three cuttings. Maximum fluopyram residues in/on alfalfa forage were 0.39 ppm at the first cutting, 0.10 ppm at the second cutting, and 0.19 ppm at the third cutting. Maximum fluopyram residues in/on alfalfa hay were 0.93 ppm at the first cutting, 0.36 ppm at the second cutting, and 0.46 ppm at the third cutting.

*Conclusions - Alfalfa*. The extensive alfalfa field rotational crop study is adequate to satisfy data requirements. Geographic representation of data is adequate; the location and number of field trials are in compliance with EPA geographic representation requirements for use on alfalfa. The data indicate that rotational crop tolerances for alfalfa forage and hay are needed to support the proposed 14-day PBI for alfalfa. The appropriate tolerance levels were calculated using the data from the first cutting; the data support tolerances of 0.45 ppm for rotated alfalfa forage and 1.1 ppm for rotated alfalfa hay (see Appendix II).

Cotton (MRID 47567125): A total of 11 field trials were conducted during the 2007 growing season to measure the magnitude of fluopyram residues in cotton seed and gin byproducts planted as a rotational crop following crops treated with fluopyram. Trials were conducted in Zone 2 (NC), 4 [AR (2), LA], 6 (TX), 8 [KS, TX(2)], and 10 [CA(3)]. The petitioner noted that a twelfth trial was initiated but then cancelled due to crop failure; it is due to be repeated.

Two foliar spray applications of the 4.16 lb/gal SC formulation (AE C656948 500 SC) were made to a cover crop or bare soil at a target rate of 0.223 lb ai/A/application (0.218 to 0.230 lb ai/A/application) for a total target application rate of 0.446 lb ai/A (0.442 to 0.456 lb ai/A or 0.495 to 0.511 kg ai/ha; 1x the proposed maximum seasonal rate to annual crops). The interval between applications was 1-5 days. Cotton was planted at each site at a target PBI of 14 days; the actual PBI ranged from 12 to 14 days. All applications were made using ground-based equipment.

At each trial, single untreated and duplicate treated samples of rotated seed cotton were collected at the normal harvest time (growth stage BBCH 89/99). The petitioner stated that cotton was harvested using either a mechanical picker (three trials), mechanical stripper (two trials), or by hand (six trials). Samples were ginned at the trial site (one trial) or at a ginning facility.

Samples of undelinted cotton seed and gin byproducts were analyzed for residues of the parent compound using an adequate HPLC/MS/MS method, Method No. GM-001-P07-01. The LOQ was 0.01 ppm in alfalfa forage and hay. Sample storage conditions and durations are reported in Table 7; samples were stored frozen for up to ~7 months prior to analysis. The available storage stability data support the field rotational crop study.

The results of the field rotational crop studies are summarized in Table 29. Residues of fluopyram were below the LOQ in/on all undelinted cotton seed samples. Quantifiable residues were found in/on cotton gin byproducts, at 0.02 ppm in/on four out of ten samples.

*Conclusions - Cotton*. The extensive cotton field rotational crop study is adequate to satisfy data requirements pending submission of the repeat field study. Geographic representation of data is adequate for cottonseed; the location and number of field trials are in compliance with HED requirements for a use on cotton since the pesticidal use resulted in no quantifiable residues. The data indicate that rotational crop tolerances for cotton undelinted seed and gin byproducts are needed to support the proposed 14-day PBI for cotton. The data support an interim inadvertent tolerance of 0.01 ppm for cotton undelined seed and 0.05 ppm for gin byproducts (see Appendix II).

Limited field rotational crop study (MRID 47567123): A limited rotational crop study with an 8-month PBI was conducted to measure the magnitude of fluopyram residues in wheat, turnip, and mustard green planted as rotational crops following cover crops treated with fluopyram. A total of 3 field trials were conducted in Zone 3 (FL), 4 (MS), and 10 (CA) during the 2007 growing season. Two foliar spray applications of the 4.16 lb/gal SC formulation (AE C656948 500 SC) were made to cover crops at a target rate of 0.223 lb ai/A/application (0.216 to 0.229 lb ai/A/application) for a total target application rate of 0.446 lb ai/A (0.440 to 0.467 lb ai/A or 0.493 to 0.525 kg ai/ha); 1x the proposed maximum seasonal rate to annual crops. The interval between applications was 5-7 days. Rotational crops of mustard greens, turnips, and wheat were planted at each site at a target PBI of 240 days; the actual PBI ranged from 228 to 248 days. At each trial, a single control and duplicate treated samples of rotated turnip (tops and roots), mustard greens (leaves), and wheat (forage, hay, grain, and straw) were collected at normal commercial maturity. Wheat hay was allowed to dry in the field or under shelter according to local practice.

The samples were analyzed for residues of the parent compound using an adequate HPLC/MS/MS method, Method No. GM-001-P07-01. The LOQ was 0.01 ppm for each rotated crop commodity. Sample storage conditions and durations are reported in Table 7; samples were stored frozen for up to ~13 months prior to analysis. The available storage stability data support the field rotational crop study.

The results of the limited field rotational crop studies are summarized in Table 29. Quantifiable residues of fluopyram were found in/on turnip tops (up to 0.04 ppm), mustard greens (up to 0.04 ppm), wheat forage (up to 0.05 ppm), wheat hay (up to 0.09 ppm), and wheat straw (up to 0.12 ppm). Residues were below the LOQ in/on all samples of rotated turnip root and wheat grain.

In addition, limited EU field rotational studies were conducted on carrot or turnip, head lettuce, and wheat in Germany, France, Italy and Spain with PBI's ranging from 28-49 days. The wheat field rotational crop trials showed maximum fluopyram levels of 0.01 ppm in wheat grain, 0.12 ppm in wheat forage, and 0.28 ppm in wheat straw when sampled at 30 day PBI (MRID 47372633).

*Conclusions - Limited field rotational crop study.* The submitted limited rotational crop study indicates the potential for quantifiable fluopyram residues in/on crops rotated 8 months following fluopyram application. Other than alfalfa and cotton (PBI of 14 days), and those crops on the label, extensive field rotational crop studies and rotational crop tolerances are required to support the rotation to canola, cereal grains except rice, corn, and soybean following application of fluopyram to potato and dry beans.

In the submission of January 24, 2011 (Revised Portfolio for Fluopyram), the registrant acknowledged that additional rotational crop data are needed to set rotational crop tolerances. In the absence of sufficient rotational crop data, the registrant suggested to use the highly conservative target crop residue data for setting rotational crops tolerances. The issue was submitted to ChemSAC for advice and the option was to examine the confined accumulation data, limited field rotational crop data, and primary crop data for the target rotated crops, and select an intermediate level so as to discourage potential misuse (i.e., direct foliar application) and provide adequate maximum residue levels for legal uses according to label instructions (ChemSAC minutes, 2/9/2011).

The residue data in canola, soybean and cereal grains except rice resulting from foliar applications for setting tolerances are described in Appendix III. Wheat is the only crop among the cereal grains that contains foliar, limited field rotational, and confined accumulation data.

When compared to the confined accumulation and limited field rotational crop data, the foliar residues in wheat commodities range from 2.7x (wheat straw) to 76x (wheat grain). Thus, HED recommends rotational crop tolerances be set at half of the calculated primary crop tolerances with a PBI of 30 days: canola seed at 1.8 ppm, soybean seed at 0.10 ppm, soybean forage at 4.0 ppm, soybean hay at 15 ppm, cereal grains group 15 (except rice), at 1.5 ppm, and forage at 4.0 ppm, hay at 6.5 ppm, and straw and stover at 7.0 ppm of cereal grains group 16 (except rice). These tolerance levels may be revised upon review of extensive field rotational crop data.

In addition, since the confined accumulation data reflect a maximum PBI of 280 days when TRR's in some crop matrices still exceeded 0.01 ppm, rotation to crops other than those discussed above is not supported.

**860.1550 Proposed Tolerances**

Bayer CropScience has proposed that the residue of concern for tolerance expression in crop commodities is fluopyram, and that the residues of concern for tolerance expression in livestock commodities are fluopyram and its metabolite AE C656948-benzamide, expressed as parent equivalents. HED has concluded that the proposed tolerance expressions are appropriate.

Codex MRLs are established for residues of fluopyram in cucumber (0.5 ppm), grapes (2 ppm), dried grapes (5 ppm), milks (0.07 ppm), and edible offal (0.7 ppm).

The tolerances proposed by Bayer CropScience are listed in Table 30, along with the tolerance levels recommended by HED. As indicated at the beginning of the document, the registrant has withdrawn the following crops or crop groups from the petition: CG 1B Root veg and 1C Tuberous and corm veg (except potatoes and sugarbeet), CG2 Leaves of root and tuberous veg CG3-07A&B Bulb veg, CG4 Leafy veg, CG5 Brassica, CG6A Edible legumes, CG6B Succulent beans and peas, CG6C (part) Dried peas (and some dried beans), CG7 Foliage of legume veg, CCG8 Fruiting veg, CG9 Cucurbit veg (except watermelon), CG10 Citrus, CG11 Pome fruit (except apple), CG12 Stone fruit (except cherry), CG13-07A&B Caneberries and Bushberries, CG13-07F Vine fruit (except wine grapes), CG13-07G Low growing berries (except strawberry), CG15 Cereal Grains (except for rotational purposes), CG16 Forage Cereals (except for rotational purposes), CG17 Grasses grown for forage or seed, CG18 Non grass animal feeds, CG19 Herbs and Spices, CG20 Oilseeds (except canola), Hops, Globe artichoke, Christmas Trees, Turf and Ornamentals. The Agency's *Guidance for Setting Pesticide Tolerances Based on Field Trial Data* was utilized for determining appropriate tolerance levels for raw agricultural crop commodities; see Appendix II for tolerance calculations.

Adequate field trial data are available to support the proposed uses on apple, cucurbit vegetables (including watermelon), dried beans, peanut, potato, stone fruit (including cherry), strawberry, sugar beet, tree nuts, and wine grapes. The proposed tolerances are appropriate for: almond, hulls; tree nuts; peanut hay; and cucurbit vegetables. The proposed tolerances are too high for sugar beet root, cotton undelinted seed, peanut, and stone fruit group 12, and HED recommends that tolerances at 0.04 ppm, 0.01 ppm, 0.02 ppm, and 0.70 ppm, respectively, be established. No tolerances have been proposed for apple; beet, sugar, tops; dried beans; grape, wine; potato; and strawberry, and tolerances for these commodities are needed. HED recommends that tolerances at 0.30 ppm, 15 ppm, 0.09 ppm, 1.4 ppm, 0.02 ppm, and 1.5 ppm, respectively, be established for apple; beet, sugar, tops; dried beans; grape, wine; potato; and strawberry.

The petitioner proposed a tolerance for "nut, tree, group 14 (including pistachio)" at 0.05 ppm. Separate tolerances must be proposed for the tree nut crop group and pistachio. The available data indicate that 0.05 ppm is an appropriate level for these tolerances.

Pending submission of information confirming that the proposed use of fluopyram on bananas to be imported into the U.S. conforms to the use patterns of the submitted banana field trial data, adequate data are available to support the proposed tolerance on banana.

The available processing data indicate that the proposed tolerance is appropriate for cotton gin byproducts. Tolerances for fluopyram residues are needed for wet apple pomace and processed potato waste. The available data indicate that the proposed tolerances are too high and that lower tolerances are needed, at 0.60 ppm for apple wet pomace and 0.08 ppm for processed potato waste. No tolerances are needed for the remaining processed commodities.

Pending submission of one additional/repeat study with rotated cotton, adequate field rotational crop data are available for rotated alfalfa and cotton commodities. The proposed tolerance for cotton gin byproducts is adequate. However, the proposed tolerances for alfalfa forage and hay are too low and the proposed tolerance for undelinted cotton seed is too high; tolerances of 0.45 ppm, 1.1 ppm, and 0.01 ppm would be appropriate for alfalfa forage, alfalfa hay, and undelinted cotton seed, respectively. In addition, the tolerances for alfalfa and cotton commodities must be revised to be specified in terms of indirect or inadvertent residues of fluopyram.

The revised label also permits crop rotation to canola, cereal grains (except rice) and soybean after treating dried beans and potato. However, extensive field rotational crop data for these crops are not available. In the absence of sufficient rotational crop data, the registrant suggested to use the highly conservative target crop residue data for setting rotational crops tolerances. The preference would be to select an intermediate level between the confined accumulation/ limited field rotational crop data and primary crop data for the target rotated crops so as to discourage potential misuse (i.e., direct foliar application) and provide adequate maximum residue levels for legal uses according to label instructions. Thus, HED recommends rotational crop tolerances be set at half of the calculated primary crop tolerances with a PBI of 30 days: canola seed at 1.8 ppm, soybean seed at 0.10 ppm, soybean forage at 4.0 ppm, soybean hay at 15 ppm, cereal grains group 15 (except rice) at 1.5 ppm, and forage at 4.0 ppm, hay at 6.5 ppm, and straw and stover at 7.0 ppm of cereal grains group 16 (except rice). These tolerances may be revised upon review of extensive field rotational crop data.

The petitioner has proposed tolerances for combined residues of fluopyram and AE C656948-benzamide in egg; milk; the fat, meat, and meat byproducts of poultry; and the fat, liver, meat, and meat byproducts (except liver) of cattle, goat, hog, horse, and sheep. The estimated livestock dietary burden and available feeding study data indicate that most of the proposed tolerances for livestock commodities are too low. In addition, HED no longer establishes separate tolerances for liver.

The recommended tolerances for plant and livestock commodities are presented in Table 30.

| **Table 30.** **Tolerance Summary for Fluopyram.** | | | |
|---|---|---|---|
| Commodity | Proposed Tolerance (ppm) | Recommended/ Harmonized Tolerance (ppm) | Comments; *Correct Commodity Definition* |
| (a)(1) It is recommended that tolerances be established for residues of the fungicide fluopyram (*N*-[2-[3-chloro-5-(trifluoromethyl)-2-pyridinyl]ethyl]-2-(trifluoromethyl)benzamide), including its metabolites and degradates, in or on the commodities below. Compliance with the tolerance levels specified below is to be determined by measuring only fluopyram in or on the commodity. | | | |
| Almond, hulls | 8.0 | 8.0 | *Almond, hull* |
| Apple | 0.5 | 0.30 | |
| Apple, wet pomace | 2.5 | 0.60 | |
| Banana (Import) | 1.0 | 1.0 | Tolerance must include a footnote stating "No U.S. registrations as of [date of FR notice]." |
| Beet, sugar, roots | 0.10 | 0.04 | *Beet, sugar, root* |
| Beet, sugar, tops | 30 | Remove | Tolerance is not required. |
| Cherry | 1.5 | 0.60 | |
| Grape, wine | 2.0 | 2.0 | |
| Nut, tree, group 14 and pistachio | 0.05 | 0.05 | *Nut, tree, group 14*<br>A separate tolerance is needed for pistachio; see below |
| Peanut | 0.05 | 0.02 | |
| Pistachio | | 0.05 | A separate tolerance is needed for pistachio. |
| Potato | 0.05 | 0.02 | |
| Potato, processed potato waste | 0.15 | 0.08 | |
| Strawberry | 2.0 | 1.5 | |
| Watermelon | 1.0 | 1.0 | |
| Vegetable, bean, dried, shelled (except soybean) | 0.50 | 0.09 | *Bean, dry* |
| (a)(2) It is recommended that tolerances be established for residues of the fungicide fluopyram (*N*-[2-[3-chloro-5-(trifluoromethyl)-2-pyridinyl]ethyl]-2-(trifluoromethyl)benzamide), including its metabolites and degradates, in or on the commodities below. Compliance with the tolerance levels specified below is to be determined by measuring only the sum of fluopyram and its metabolite 2-(trifluoromethyl)benzamide, calculated as the stoichiometric equivalent of fluopyram, in or on the commodity. | | | |
| Cattle, fat | 0.10 | 0.11 | |
| Cattle, meat | 0.10 | 0.15 | |
| Cattle, meat byproducts, except liver | 0.10 | 1.1 | *Cattle, meat byproducts* |
| Cattle, liver | 1.2 | | |
| Eggs | 0.10 | 0.25 | *Egg* |
| Goat, fat | 0.10 | 0.11 | |
| Goat, meat | 0.10 | 0.15 | |
| Goat, meat byproducts, except liver | 0.10 | 1.1 | *Goat, meat byproducts* |
| Goat, liver | 1.2 | | |
| Hog, fat | 0.01 | 0.05 | |
| Hog, meat | 0.01 | 0.05 | |

| **Table 30.** **Tolerance Summary for Fluopyram.** | | | |
|---|---|---|---|
| Commodity | Proposed Tolerance (ppm) | Recommended/ Harmonized Tolerance (ppm) | Comments; *Correct Commodity Definition* |
| Hog, meat byproducts, except liver | 0.01 | 0.70 | *Hog, meat byproducts* |
| Hog, liver | 0.15 | | |
| Horse, fat | 0.10 | 0.11 | |
| Horse, meat | 0.10 | 0.15 | |
| Horse, meat byproducts, except liver | 0.10 | 1.1 | *Horse, meat byproducts* |
| Horse, liver | 1.2 | | |
| Milk | 1.2 | 0.07 | |
| Poultry, fat | 0.05 | 0.20 | |
| Poultry, meat | 0.03 | 0.15 | |
| Poultry, meat byproducts | 0.20 | 0.60 | |
| Sheep, fat | 0.10 | 0.11 | |
| Sheep, meat | 0.10 | 0.15 | |
| Sheep, meat byproducts, except liver | 0.10 | 1.1 | *Sheep, meat byproducts* |
| Sheep, liver | 1.2 | | |
| (d) It is recommended that tolerances be established for indirect or inadvertent residues of fungicide fluopyram (*N*-[2-[3-chloro-5-(trifluoromethyl)-2-pyridinyl]ethyl]-2-(trifluoromethyl)benzamide), including its metabolites and degradates, in or on the commodities below. Compliance with the tolerance levels specified below is to be determined by measuring only fluopyram in or on the commodity. | | | |
| Alfalfa, forage | 0.25 | 0.45 | |
| Alfalfa, hay | 0.80 | 1.1 | |
| Canola, seed | 5.0 | 1.8 | |
| Corn, sweet, kernel plus cob with husk removed | 0.10 | Remove | Tolerance is covered under *Grain, cereal, group 15, except rice;* see below |
| Cotton, gin byproducts | 0.05 | 0.05 | |
| Cotton, undelinted seed | 0.10 | 0.01 | |
| Grain, cereal, forage, fodder and straw, group 16, except rice; forage | 8.0 | 4.0 | |
| Grain, cereal, forage, fodder and straw, group 16, except rice; hay, straw and stover | 14 | 7.0 | |
| Grain, cereal, forage, fodder and straw, group 16, except rice; aspirated fractions | 50 | Remove | Tolerance is not applicable. |
| Grain, cereal, group 15, except rice and sweet corn | 3.0 | 1.5 | *Grain, cereal, group 15, except rice* |
| Soybean, forage | 8.0 | 4.0 | |
| Soybean, hay | 30 | 15 | |
| Soybean, hulls | 0.40 | Remove | Tolerance is not applicable. |
| Soybean, seed | 0.30 | 0.10 | |

## References

Attachments:
International Residue Limits
Appendix I – Summary of Fluopyram and Metabolites
Appendix II - Tolerance Assessment Calculations
Appendix III - Tolerance Assessment Calculations (for “rotated crops” except alfalfa and cotton)

Template Version September 2005

# International Residue Limits

## Fluopyram (080302; 06/06/2011)

| Summary of US and International Tolerances and Maximum Residue Limits | | | | |
|---|---|---|---|---|
| *Residue Definition*: | | | | |
| US | | Canada | Mexico[2] | Codex[3] |
| 40 CFR 180.XXX:<br>Plants: fluopyram (N-[2-[3-chloro-5-(trifluoromethyl)-2-pyridinyl]ethyl]-2-(trifluoromethyl)benzamide).<br><br>Livestock: sum of fluopyram (N-[2-[3-chloro-5-(trifluoromethyl)-2-pyridinyl]ethyl]-2-(trifluoromethyl)benzamide) and its benzamide metabolite [2-(trifluoromethyl)-benzamide], calculated as the stoichiometric equivalent of fluopyram | | Identical to US | | Plants: fluopyram.<br>Animal commodities: Sum of fluopyram and 2-(trifluoromethyl)benzamide, expressed as fluopyram. |
| *Commodity[1]* | *Tolerance (ppm) /Maximum Residue Limit (mg/kg)* | | | |
| | US | Canada | Mexico[2] | Codex[3] |
| Almond hull | 8.0 | | | |
| Apple | 0.30 | | | |
| Apple wet pomace | 0.60 | | | |
| Banana (import) | 1.0 | | | |
| Bean, dry | 0.09 | | | |
| Cherry | 0.60 | | | |
| Nut, tree, group 14 | 0.05 | | | |
| Peanut | 0.02 | | | |
| Pistachio | 0.05 | | | |
| Potato | 0.02 | | | |
| Potato processed waste | 0.08 | | | |
| Strawberry | 1.5 | | | |
| Sugar beet | 0.04 | | | |
| Watermelon | 1.0 | | | |
| Wine Grapes | 2.0 | | | 5 Dried grapes (=currants, raisins and sultanas) ; 2 Grapes |
| | | | | |
| Alfalfa forage | 0.45 | | | |
| Alfalfa hay | 1.1 | | | |
| Canola seed | 1.8 | | | |
| Cotton gin byproducts | 0.05 | | | |
| Cotton undelinted seed | 0.01 | | | |
| Grain, cereal, group 15, except rice | 1.5 | | | |
| Grain, cereal, forage, fodder and straw, group 15, except rice; forage | 4.0 | | | |
| Grain, cereal, forage, fodder and straw, group 15, except rice; hay, straw and stover | 7.0 | | | |
| Soybean forage | 4.0 | | | |
| Soybean hay | 15 | | | |
| Soybean seed | 0.10 | | | |
| | | | | |

| Summary of US and International Tolerances and Maximum Residue Limits | | | | |
|---|---|---|---|---|
| *Residue Definition*: | | | | |
| US | | Canada | Mexico[2] | Codex[3] |
| Cattle, fat | 0.11 | | | |
| Cattle, meat | 0.15 | | | 0.1 Meat (from mammals other than marine mammals) |
| Cattle, meat byproducts | 1.1 | | | 0.7 Edible offal (mammalian) |
| Eggs | 0.25 | | | |
| Goat, fat | 0.11 | | | |
| Goat, meat | 0.15 | | | |
| Goat, meat byproducts | 1.1 | | | |
| Hog, fat | 0.05 | | | |
| Hog, meat | 0.05 | | | |
| Hog, meat byproducts | 0.70 | | | |
| Horse, fat | 0.11 | | | |
| Horse, meat | 0.15 | | | |
| Horse, meat byproducts | 1.1 | | | |
| Milk | 0.07 | | | Milks 0.07 |
| Poultry, fat | 0.20 | | | |
| Poultry, meat | 0.15 | | | |
| Poultry, meat byproducts | 0.60 | | | |
| Sheep, fat | 0.11 | | | |
| Sheep, meat | 0.15 | | | |
| Sheep, meat byproducts | 1.1 | | | |

[1] Includes only commodities of interest for this action. Tolerance values should be the HED recommendations and not those proposed by the applicant.

[2] Mexico adopts US tolerances and/or Codex MRLs for its export purposes.

[3] * = absent at the limit of quantitation; Po = postharvest treatment, such as treatment of stored grains. PoP = processed postharvest treated commodity, such as processing of treated stored wheat. (fat) = to be measured on the fat portion of the sample. MRLs indicated as proposed have not been finalized by the CCPR and the CAC.